

FOR OFFICIAL USE ONLY  
ACCESS DB # \_\_\_\_\_

PLEASE PRINT CLEARLY  
Location (Bldg/Room#): 4124G

Scientific and Technical Information Center  
SEARCH REQUEST FORM

Date: 4/27/98 Requester's Full Name: Grace Hsu Examiner #: 77391  
Art Unit: 1622 Phone (305) 7005 Serial Number: 09/148,933  
Results Format Preferred (circle):  PAPER  DISK  E-MAIL

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Method of Administering An APTA Resevoir Antagonist  
Inventors (please provide full names): Lee T. Hsu

Earliest Priority Date: 9/24/98

Search Topic:

*Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known.*

*For Sequence Searches Only\* Please include all pertinent information (parent, grandchild, divisional, or issued patent numbers) along with the appropriate serial number.*

*Please Search Claims 1-9*

*① Lee P 4/27/98 APTA resevoir  
Antagonist*

*09/148,933*

*pwk*

STAFF USE ONLY

Searcher: Qan

Searcher Phone #: 4498

Searcher Location: 4124G

Date Searcher Picked Up: 4/20

Date Completed: 4/20

Searcher Prep & Review Time: 15

Online Time: +60

Type of Search

NA Sequence (#)

AA Sequence (#)

Structure (#)

Bibliographic

Litigation

Fulltext

Other

Vendors and Cost

STN  Dialog

Questel/Orbit  Dr. Link

Lexis/Nexis  Westlaw

WWW/Internet

In-house sequence systems (list)

Other (specify)

=> d his

(FILE 'HOME' ENTERED AT 16:10:22 ON 30 APR 2001)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 16:10:35 ON 30 APR 2001  
E GREENAMYRE J/AU  
L1 80 S E4-E10  
E CHENARD B/AU  
L2 73 S E4-E9  
E WELCH W/AU  
L3 15 S E3,E14  
L4 73 S E20-E25  
E MENNITI F/AU  
L5 38 S E4-E7  
L6 252 S L1-L5  
L7 22 S L6 AND AMPA  
L8 10 S L6 AND AMINO(L)HYDROXY(L)METHYL(L)ISOXAZOL?

FILE 'REGISTRY' ENTERED AT 16:14:04 ON 30 APR 2001  
L9 1 S 77521-29-0

FILE 'HCAPLUS' ENTERED AT 16:14:10 ON 30 APR 2001  
L10 1054 S L9  
2 S L6 AND L10  
L11 24 S L7,L8,L11  
L13 1 S L6 AND DIETHYLAMINOMETHYL PYRIDIN? (L) QUINAZOL?

FILE 'REGISTRY' ENTERED AT 16:16:00 ON 30 APR 2001  
L14 1 S 59-92-7  
E D-TYROSINE, 3-HYDROXY-/CN  
L15 1 S E3  
E DL-TYROSINE, 3-HYDROXY-/CN  
L16 1 S E3  
L17 1 S 28860-95-9  
E C10H14N2O4/MF  
L18 5 S E3 AND BENZENEPROPANOIC AND HYDRAZIN?  
L19 3 S L18 NOT (ESTER OR 5 DIHYDROXY)  
L20 1 S 322-35-0  
E C10H15N3O5/MF  
L21 5 S E3 AND 46.150.18/RID AND SERINE AND TRIHYDROXYPHENYL  
L22 5 S L21 AND HYDRAZ?  
L23 4 S L22 NOT 5  
L24 3 S L23 NOT 4228-70-0  
L25 1 S 199655-81-7  
L26 1 S 199655-81-7/CRN

FILE 'HCAOLD' ENTERED AT 16:21:33 ON 30 APR 2001  
L27 0 S L25 OR L26

FILE 'HCAPLUS' ENTERED AT 16:21:37 ON 30 APR 2001  
L28 4 S L25 OR L26  
4 S L28 AND L6  
L29 1 S L28 AND L10  
L30 4 S L28 AND AMPA  
L31 4 S L28-L31

FILE 'REGISTRY' ENTERED AT 16:23:03 ON 30 APR 2001  
L33 3 S L14-L16  
SEL RN  
L34 95 S E1-E3/CRN  
L35 3 S L17,L19  
SEL RN  
L36 22 S E4-E6/CRN  
L37 3 S L20,L24  
SEL RN

Point of Contact:  
Jan Delaval  
Librarian-Physical Sciences  
CM1 1E01 Tel: 308-4498

L38 8 S E7-E9/CRN  
 L39 7 S L34 AND L36, L38  
 L40 2 S L39 AND 2/NC  
 L41 7 S L38 NOT L40

FILE 'HCAPLUS' ENTERED AT 16:24:25 ON 30 APR 2001  
 L42 102 S L40  
 L43 9797 S L33  
 L44 14549 S DOPA OR LEVODOPA  
 L45 15989 S L43, L44  
 L46 843 S L35 OR L37  
 L47 1209 S BENSERAZIDE OR CARBIDOPA  
 L48 1496 S L46, L47  
 L49 1085 S L45 AND L48  
 L50 1127 S L42, L49  
 L51 3 S L50 AND L10  
 L52 6 S L50 AND AMPA  
 L53 0 S L50 AND (AMINO(L)HYDROXY(L)METHYL(L)ISOXAZOL?)  
 L54 6 S L51, L52  
 L55 2 S L54 AND L32  
 L56 2 S L31 AND L45, L48  
 L57 2 S L55, L56

FILE 'REGISTRY' ENTERED AT 16:28:34 ON 30 APR 2001  
 L58 1 S 9042-64-2

FILE 'HCAPLUS' ENTERED AT 16:28:40 ON 30 APR 2001  
 L59 1 S L32 AND L58  
 L60 1 S L32 AND ?DECARBOXYLASE?  
 L61 4 S L32, L57, L59, L60  
 L62 12 S L42 AND DYSKINES?  
 L63 3 S L42 AND TREMOR?  
 L64 49 S L42 AND ?PARKINSON?  
 L65 4 S L42 AND (CHOREA OR BALLISM OR DYSTON? OR ATHETO? OR MYOCLONUS  
 L66 6 S L42 AND MOTOR  
 L67 0 S L62-L66 AND L61  
 E DYSKINES/CT  
 E E5+ALL  
 L68 48 S E1  
 L69 774 S E2  
 E DYSKINES/CW  
 L70 136 S E4  
 L71 2 S L61 AND L68-L70  
 L72 4 S L61, L71  
 L73 14 S L64 AND L62, L63, L65, L66, L68-L70  
 L74 16997 S NMDA  
 L75 4925 S KAINIC ACID

FILE 'REGISTRY' ENTERED AT 16:37:48 ON 30 APR 2001  
 L76 2 S 6384-92-5 OR 487-79-6  
 E L-ASPARTIC ACID, N-METHYL-/CN  
 L77 1 S E3  
 E DL-ASPARTIC ACID, N-METHYL-/CN  
 L78 1 S E3  
 E 3-PYRROLIDINEACETIC ACID, 2-CARBOXY-4-(1-METHYLETHENYL)-/CN  
 L79 1 S E3  
 E C10H15NO4/MF  
 L80 11 S E3 AND PYRROLIDINEACETIC AND CARBOXY AND METHYLETHENYL  
 L81 10 S L80 NOT T/ELS

FILE 'HCAPLUS' ENTERED AT 16:40:21 ON 30 APR 2001  
 L82 8562 S L76-L79, L81  
 L83 11908 S N() (METHYLASPARTIC OR METHYLASPARTATE OR METHYL(1W) (ASPARTIC  
 E GLUTAMATE RECEPTOR/CT  
 E E5+ALL  
 L84 7753 S E8+NT

L85 25779 S L74,L75,L82-L84  
 L86 109 S SINEMET OR MADOPAR  
 L87 137 S L42,L86  
 L88 1 S L87 AND L85  
 L89 0 S L87 AND (L10 OR AMPA)

FILE 'USPATFULL' ENTERED AT 16:44:15 ON 30 APR 2001  
 L90 1 S L25,L26

=> fil hcaplus  
 FILE 'HCAPLUS' ENTERED AT 16:44:40 ON 30 APR 2001  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1947 - 30 Apr 2001 VOL 134 ISS 19  
 FILE LAST UPDATED: 29 Apr 2001 (20010429/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

=> d all hitstr tot 172

L72 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1999:175749 HCAPLUS  
 DN 130:218317  
 TI AMPA antagonists for the treatment of dyskinesias associated with dopamine agonist therapy  
 IN Chenard, Bertrand Leo; Menniti, Frank Samuel;  
 Welch, Willard McKowan, Jr.  
 PA Pfizer Products Inc., USA  
 SO Eur. Pat. Appl., 22 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 IC ICM A61K031-505  
 ICI A61K031-505, A61K031-195, A61K031-15  
 CC 1-11 (Pharmacology)  
 Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900568	A2	19990310	EP 1998-307181	19980904
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 11158072	A2	19990615	JP 1998-245269	19980831
	AU 9883120	A1	19990318	AU 1998-83120	19980904
	US 6136812	A	20001024	US 1998-148974	19980904
	CA 2246839	AA	19990305	CA 1998-2246839	19980908
PRAI	US 1997-58098	P	19970905		

OS MARPAT 130:218317

AB The invention relates to a method of treating dyskinesias assocd. with dopamine agonist therapy in a mammal which comprises administering to said mammal a compd., as defined herein, which is an antagonist of the **AMPA** receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease. One example compd. of the 212 claimed was (S)-3-(2-chlorophenyl)-2-[2-(5-diethylaminomethyl-2-fluorophenyl)vinyl]-6-fluoro-3H-quinazolin-4-one.

ST **AMPA** antagonist dyskinesia dopamine agonist

IT Drug delivery systems

Parkinson's disease

(**AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **AMPA** receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **Dyskinesia (nervous system)**

(Parkinson's-assocd.; **AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 51-61-6, Dopamine, biological studies 59-92-7, biological studies 322-35-0, **Benserazide** 3257-47-4**28860-95-9, Carbidopa** 199655-53-3 199655-54-4

199655-56-6 199655-57-7 199655-58-8 199655-59-9 199655-61-3

199655-62-4 199655-63-5 199655-64-6 199655-65-7 199655-66-8

199655-67-9 199655-68-0 199655-69-1 199655-70-4 199655-71-5

199655-72-6 199655-75-9 199655-76-0 199655-77-1 199655-78-2

199655-80-6 **199655-81-7** 199655-82-8 199655-84-0

199655-86-2 199655-87-3 199655-88-4 199655-89-5 199655-90-8

199655-91-9 199656-00-3 199656-44-5 212710-60-6 212710-61-7

212710-62-8 212710-64-0 212710-65-1 212710-66-2 212710-70-8

212765-03-2 212850-63-0 212850-64-1 212850-72-1 212850-74-3

212850-78-7 212850-79-8 212850-80-1 212850-81-2 212850-82-3

212916-59-1 212916-65-9 217821-32-4 217821-33-5 217821-34-6

217821-35-7 217821-36-8 217821-37-9 217821-38-0 217821-39-1

217821-41-5 217821-42-6 217942-51-3 217942-54-6 217942-55-7

217942-57-9 217942-58-0 217942-60-4 217942-62-6 217942-63-7

217942-64-8 217942-66-0 217942-68-2 217942-69-3 217942-71-7

217942-72-8 217942-74-0 217942-76-2 217942-78-4 217942-86-4

217942-87-5 221151-74-2 221151-75-3 221151-81-1 221151-83-3

221151-84-4 221151-88-8 221151-95-7 221152-14-3 221152-18-7

221152-21-2 221152-23-4 221152-26-7 221152-29-0 221152-30-3

221152-31-4 221152-32-5 221152-34-7 221152-35-8 221152-36-9

221152-37-0 221152-38-1 221152-39-2 221152-40-5 221152-41-6

221152-42-7 221152-43-8 221152-44-9 221152-45-0 221152-46-1

221152-47-2 221152-48-3 221152-49-4 221152-50-7 221152-51-8

221152-52-9 221152-53-0 221152-54-1 221152-55-2 221152-56-3

221152-57-4 221152-58-5 221152-59-6 221152-60-9 221152-61-0

221152-62-1 221152-63-2 221167-22-2 221167-24-4 221167-27-7

221167-29-9 221167-33-5 221167-37-9 221167-44-8 221167-46-0

221167-49-3 221167-52-8 221167-54-0 221167-56-2 221167-59-5

221167-62-0 221167-63-1 221167-65-3 221167-66-4 221167-68-6

221167-70-0 221167-72-2 221167-73-3 221167-74-4 221167-75-5

221167-78-8 221167-79-9 221167-80-2 221167-81-3 221167-82-4

221167-83-5 221167-84-6 221167-85-7 221167-92-6 221167-95-9

221167-96-0 221167-97-1 221167-99-3 221168-01-0 221168-06-5

221168-10-1 221168-22-5 221168-25-8 221168-27-0 221168-39-4

221168-41-8 221168-42-9 221168-44-1 221168-46-3 221168-49-6

221168-52-1 221168-53-2 221168-58-7 221168-61-2 221168-64-5

221168-67-8 221168-70-3 221168-72-5 221168-74-7 221168-77-0

221168-78-1 221168-80-5 221168-82-7 221168-84-9 221168-86-1

221168-88-3 221177-80-6 221177-81-7 221177-82-8 221177-83-9

221177-84-0 221177-85-1 221177-86-2 221177-87-3 221177-88-4

221177-89-5 221177-90-8 221177-91-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 77521-29-0, Ampa

RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 9042-64-2, Dopa decarboxylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 59-92-7, biological studies 322-35-0,

Benserazide 28860-95-9, Carbidopa

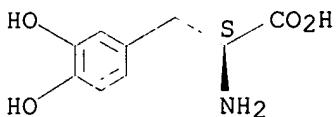
199655-81-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 59-92-7 HCPLUS

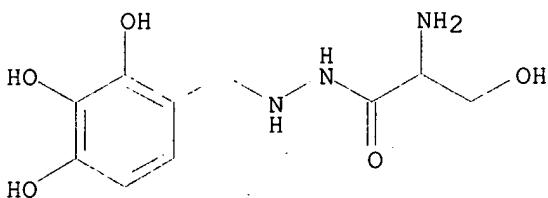
CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322-35-0 HCPLUS

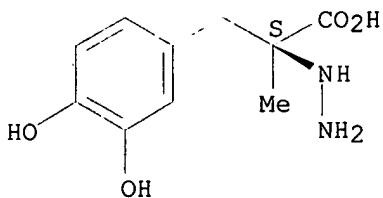
CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)



RN 28860-95-9 HCPLUS

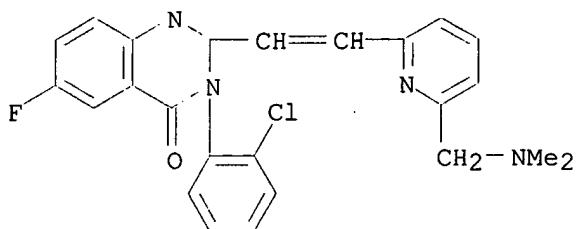
CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 199655-81-7 HCPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)

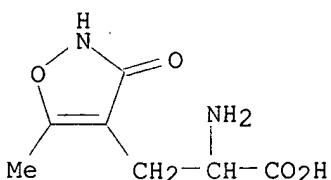


IT 77521-29-0, Ampa

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(antagonists; **AMPA** antagonists for treatment of dyskinesias  
assocd. with dopamine agonist therapy)

RN 77521-29-0 HCPLUS

CN 4-Isoxazolepropanoic acid, .alpha.-amino-2,3-dihydro-5-methyl-3-oxo- (9CI)  
(CA INDEX NAME)



IT 9042-64-2, Dopa decarboxylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; **AMPA** antagonists for treatment of dyskinesias  
assocd. with dopamine agonist therapy)

RN 9042-64-2 HCPLUS

CN Decarboxylase, aromatic amino acid (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L72 ANSWER 2 OF 4 HCPLUS COPYRIGHT 2001 ACS

AN 1999:175748 HCPLUS

DN 130:209717

TI Preparation of 3-(2-chlorophenyl)-2-[2-(6-diethylaminomethylpyridin-2-yl)vinyl]-6-fluoro-3H-quinazolin-4-one as an **AMPA** antagonist for the treatment of dyskinesias associated with dopamine agonist therapy.

IN Chenard, Bertrand Leo; Greenamyre, John Timothy;  
Menniti, Frank Samuel; Welch, Willard McKowan, Jr.

PA Pfizer Products Inc., USA

SO Eur. Pat. Appl., 6 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K031-505

ICI A61K031-505, A61K031-195, A61K031-15

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900567	A2	19990310	EP 1998-306661	19980820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2246560	AA	19990305	CA 1998-2246560	19980903
	JP 11139991	A2	19990525	JP 1998-249644	19980903
	AU 9883193	A1	19990318	AU 1998-83193	19980907

PRAI US 1997-57965 19970905

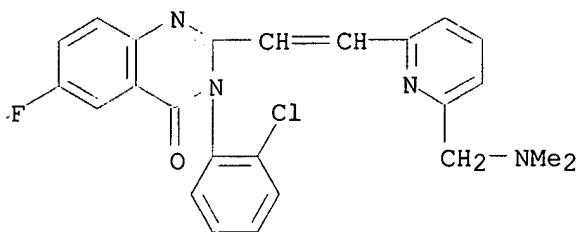
AB A method for the treatment of dyskinesias assocd. with dopamine agonist therapy comprising administration of an **AMPA** antagonist is

- claimed (no data). Thus, 3-(2-chlorophenyl)-6-fluoro-2-methyl-4-(3H)-quinazolinone (prepn. given) was refluxed with 2,6-pyridinedicarboxaldehyde, ZnCl<sub>2</sub>, and Ac<sub>2</sub>O in dioxane to give 33% 6-[2-[3-(2-chlorophenyl)-6-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl]vinyl]pyridine-2-carboxaldehyde. This was stirred with Et<sub>2</sub>NH and NaBH(AcO)<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> to give 24% title compd. as the monomaleate salt.
- ST chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolinone prepn  
**AMPA** antagonist; quinazolinone chlorophenyl diethylaminomethylpyridinylvinyl prepn **AMPA** antagonist; dyskinesia treatment  
**AMPA** antagonist chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolinone
- IT **AMPA** receptors  
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)  
 (antagonists; prepn. of chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT **Dyskinesia (nervous system)**  
 (treatment; prepn. of chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT 220931-86-2P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT 199655-81-7  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (prepn. of chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT 59-92-7, L-Dopa, miscellaneous 322-35-0,  
 Benserazide 28860-95-9, Carbidopa  
 RL: MSC (Miscellaneous)  
 (prepn. of chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT 95-51-2, 2-Chloroaniline 109-89-7, reactions 320-98-9 5431-44-7,  
 2,6-Pyridinedicarboxaldehyde  
 RL: RCT (Reactant)  
 (prepn. of chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT 38520-78-4P 49579-12-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT 220931-86-2P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of chlorophenyl diethylaminomethylpyridinylvinylfluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- RN 220931-86-2 HCPLUS  
 CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 199655-81-7

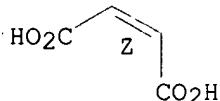
CMF C24 H20 Cl F N4 O



CM 2

CRN 110-16-7  
CMF C4 H4 04  
CDES 2:Z

Double bond geometry as shown.

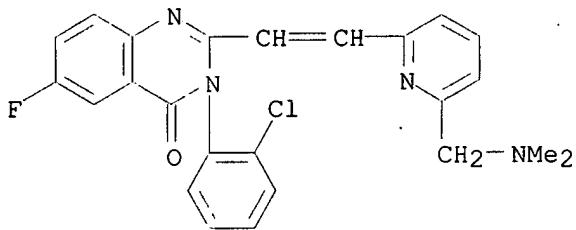


IT 199655-81-7

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prepn. of chlorophenyl-diethylamino-methyl-pyridinyl-vinyl-fluoroquinazolin-one as an **AMPA** antagonist for the treatment of dyskinésias asscoed. with dopamine agonist therapy)

RN 199655-81-7 HCAPLUS

CN 4 (3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



IT 59-92-7, L-Dopa, miscellaneous 322-35-0,  
Benserazide 28860-95-9, Carbidopa

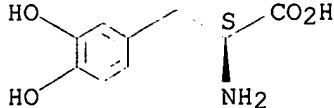
RL: MSC (Miscellaneous)

(prepn. of chlorophenyl-diethylamino-methyl-pyridinyl-vinyl-fluoro-quinazolin-one as an **AMPA** antagonist for the treatment of dyskinesias assoc'd. with dopamine agonist therapy)

RN 59-92-7 HCAPLUS

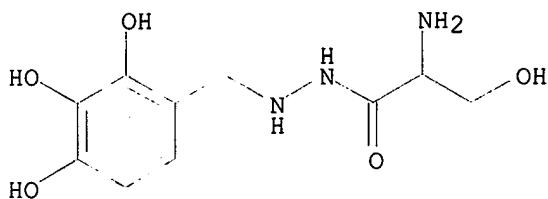
CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)

### Absolute stereochemistry.



RN 322-35-0 HCPLUS

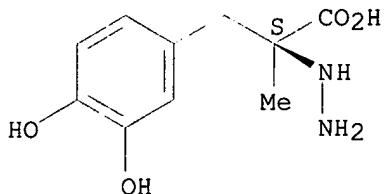
CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)



RN 28860-95-9 HCPLUS

CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L72 ANSWER 3 OF 4 HCPLUS COPYRIGHT 2001 ACS

AN 1998:608605 HCPLUS

DN 129:230733

TI Preparation of atropisomers of 3-aryl-4(3H)-quinazolinones and their use as AMPA-receptor antagonists

IN Welch, Willard McKowan, Jr.; Devries, Keith M.

PA Pfizer Products Inc., USA

SO PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D239-91

ICS C07D401-06; C07D417-06; C07D401-14; C07D405-06; C07D413-06; A61K031-505; C07M007-00

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

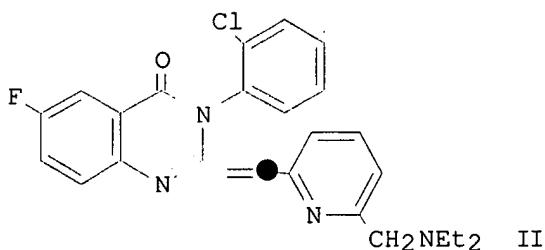
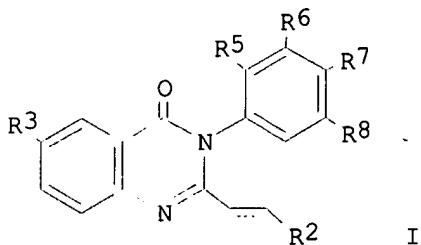
Section cross-reference(s): 1, 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
------------	------	------	-----------------	------

PI	WO 9838173	A1	19980903	WO 1998-IB150	19980206
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU	9856768	A1	19980918	AU 1998-56768	19980206
EP	968194	A1	20000105	EP 1998-900978	19980206
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR	9807872	A	20000321	BR 1998-7872	19980206
JP	2000509731	T2	20000802	JP 1998-537448	19980206
NO	9904177	A	19990827	NO 1999-4177	19990827
PRAI	US 1997-38905	P	19970228		
	WO 1998-IB150	W	19980206		

OS MARPAT 129:230733  
 GI



AB Title atropisomers [I; wherein R2 is an optionally substituted aryl or heteroaryl, R5 is alkyl, halo, CF3, alkoxy or alkylthio, R6, R7 and R8 are hydrogen or halo, and R3 is hydrogen, halo, CN, NO2, CF3, alkyl or alkoxy] are prep'd. and are useful as **AMPA** receptor antagonists, particularly in the treatment of neurodegenerative and CNS-trauma related conditions (no data). The title (S)-atropisomer II was prep'd. from 2-chloroaniline, 6-fluoro-2-methylquinoxalin-4-one which was prep'd. from hydrogenation, acetylation, and cyclization of 2-nitro-5-fluorobenzoic acid, followed by reaction with 2,6-pyridinedicarboxaldehyde, and diethylamine, and was column sepd.

ST quinazolinone prep'n; atropisomer quinazolinone sepn HPLC receptor antagonist

IT Separation

(HPLC column; prep'n. and sepn. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT **AMPA** receptors

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(antagonists; prep'n. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT 212850-63-0P 212850-64-1P 212850-65-2P 212850-66-3P 212850-68-5P  
 212850-70-9P 212850-72-1P 212850-73-2P 212850-74-3P 212850-75-4P  
 212850-76-5P 212850-77-6P 212850-78-7P 212850-79-8P 212850-80-1P  
 212850-81-2P 212850-82-3P 212916-59-1P 212916-60-4P 212916-61-5P  
 212916-62-6P 212916-63-7P 212916-64-8P 212916-65-9P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prep'n. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT 95-51-2, 2-Chloroaniline 109-89-7, Diethylamine, reactions 320-98-9  
 340-57-8 617-84-5, Diethylformamide 626-05-1, 2,6-Dibromopyridine  
 5431-44-7, 2,6-Pyridinedicarboxaldehyde 20949-84-2 27366-72-9  
 49579-01-3 49579-08-0 199656-43-4

RL: RCT (Reactant)

(prepn. of atropisomers of arylquinazolinones as **AMPA**  
-receptor antagonists)

IT 10200-43-8P 49579-12-6P 68683-04-5P 78441-69-7P 82586-66-1P  
 113732-84-6P 141567-53-5P 174608-36-7P 194473-04-6P 199599-68-3P  
 199655-35-1P 199655-36-2P 199655-54-4P 199655-55-5P 199655-57-7P  
 199655-61-3P 199655-62-4P 199655-63-5P 199655-65-7P 199655-66-8P  
 199655-67-9P 199655-68-0P 199655-69-1P 199655-70-4P 199655-71-5P  
 199655-72-6P 199655-73-7P 199655-74-8P 199655-75-9P 199655-76-0P  
 199655-77-1P 199655-78-2P 199655-79-3P 199655-80-6P  
**199655-81-7P** 199655-82-8P 199655-83-9P 199655-84-0P  
 199655-86-2P 199655-87-3P 199655-88-4P 199655-89-5P 199655-90-8P  
 199655-91-9P 199655-92-0P 199655-93-1P 199655-96-4P 199655-97-5P  
 199655-98-6P 199655-99-7P 199656-02-5P 199656-03-6P 199656-04-7P  
 199656-05-8P 199656-06-9P 199656-28-5P 199656-29-6P 199656-30-9P  
 199656-31-0P 199656-32-1P 199656-33-2P 199656-34-3P 199656-35-4P  
 199656-40-1P 212764-92-6P 212764-93-7P 212764-94-8P 212764-95-9P  
 212764-96-0P 212764-97-1P 212764-99-3P 212765-00-9P 212765-01-0P  
 212765-02-1P 212765-03-2P 212765-05-4P 212765-06-5P 212765-07-6P  
 212765-08-7P 212765-09-8P 212765-10-1P 212765-11-2P 212765-12-3P  
 212765-13-4P 212765-15-6P 212765-16-7P 212765-19-0P 212765-20-3P  
 212765-21-4P 212765-22-5P 212765-23-6P 212765-24-7P 212765-25-8P  
 212765-26-9P 212765-27-0P 212765-28-1P 212772-14-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of atropisomers of arylquinazolinones as **AMPA**  
-receptor antagonists)

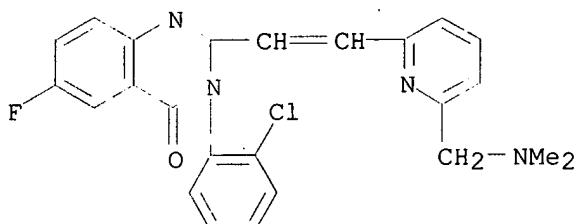
IT **199655-81-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of atropisomers of arylquinazolinones as **AMPA**  
-receptor antagonists)

RN 199655-81-7 HCPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



L72 ANSWER 4 OF 4 HCPLUS COPYRIGHT 2001 ACS

AN 1997:752948 HCPLUS

DN 128:34774

TI Preparation of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA**  
receptor antagonists.

IN Elliott, Mark Leonard; Welch, Willard Mckowan Jr

PA Pfizer Inc., USA; Elliott, Mark Leonard; Welch, Willard Mckowan Jr.

SO PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D401-06

ICS C07D401-04; C07D401-14; C07D405-06; C07D403-06; C07D239-91;  
C07D417-14; C07D417-06; A61K031-505

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

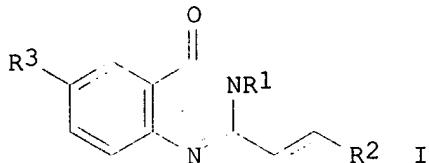
FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9743276 A1 19971120 WO 1997-IB134 19970217

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,  
 LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,  
 RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,  
 YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,  
 MR, NE, SN, TD, TG  
 CA 2252907 AA 19971120 CA 1997-2252907 19970217  
 AU 9715549 A1 19971205 AU 1997-15549 19970217  
 EP 901487 A1 19990317 EP 1997-901749 19970217  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,  
 SI, LT, LV, FI, RO  
 CN 1218464 A 19990602 CN 1997-194654 19970217  
 BR 9709085 A 19990803 BR 1997-9085 19970217  
 JP 11514663 T2 19991214 JP 1997-540682 19970217  
 ZA 9704156 A 19981116 ZA 1997-4156 19970514  
 NO 9805293 A 19990113 NO 1998-5293 19981113  
 PRAI US 1996-17738 19960515  
 WO 1997-IB134 19970217  
 OS MARPAT 128:34774  
 GI



AB Title compds. [I; R1 = (substituted) Ph, pyridyl; R2 = (substituted) Ph, 5-6 membered heterocyclyl; R3 = H, halo, cyano, NO<sub>2</sub>, CF<sub>3</sub>, alkyl, alkoxy], were prep'd. Thus, 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylvinyl)-3H-quinazolin-4-one was hydrogenated in EtOAc over Pd/C to give 100% 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylethyl)-3H-quinazolin-4-one. Tested I inhibited AMPA receptor activation-induced 45Ca<sup>2+</sup> uptake with IC<sub>50</sub> < 5 .mu.M.

ST quinazolinone prep'n AMPA receptor antagonist; nervous system agents quinazolinone

IT Nervous system agents

Neurotransmitter antagonists  
 (prep'n. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT	3257-47-4P	199655-35-1P	199655-36-2P	199655-37-3P	199655-38-4P
	199655-39-5P	199655-40-8P	199655-41-9P	199655-42-0P	199655-43-1P
	199655-44-2P	199655-45-3P	199655-46-4P	199655-47-5P	199655-48-6P
	199655-49-7P	199655-50-0P	199655-51-1P	199655-52-2P	199655-53-3P
	199655-54-4P	199655-55-5P	199655-56-6P	199655-57-7P	199655-58-8P
	199655-59-9P	199655-60-2P	199655-61-3P	199655-62-4P	199655-63-5P
	199655-64-6P	199655-65-7P	199655-66-8P	199655-67-9P	199655-68-0P
	199655-69-1P	199655-70-4P	199655-71-5P	199655-72-6P	199655-73-7P
	199655-74-8P	199655-75-9P	199655-76-0P	199655-77-1P	199655-78-2P
	199655-79-3P	199655-80-6P	199655-81-7P	199655-82-8P	
	199655-83-9P	199655-84-0P	199655-85-1P	199655-86-2P	199655-87-3P
	199655-88-4P	199655-89-5P	199655-90-8P	199655-91-9P	199655-92-0P
	199655-93-1P	199655-94-2P	199655-95-3P	199655-96-4P	199655-97-5P
	199655-98-6P	199655-99-7P	199656-00-3P	199656-01-4P	199656-02-5P
	199656-03-6P	199656-04-7P	199656-05-8P	199656-06-9P	199656-07-0P
	199656-08-1P	199656-09-2P	199656-10-5P	199656-11-6P	199656-12-7P
	199656-13-8P	199656-14-9P	199656-15-0P	199656-16-1P	199656-17-2P
	199656-18-3P	199656-19-4P	199656-20-7P	199656-21-8P	199656-22-9P
	199656-23-0P	199656-24-1P	199656-25-2P	199656-26-3P	199656-27-4P

199656-28-5P 199656-29-6P 199656-30-9P 199656-31-0P 199656-32-1P  
 199656-33-2P 199656-34-3P 199656-35-4P 199656-36-5P 199656-37-6P  
 199656-38-7P 199656-39-8P 199656-40-1P 199656-41-2P 199656-44-5P  
 199656-45-6P 199656-46-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT 95-51-2, 2-Chloroaniline 320-98-9 340-57-8 5431-44-7,  
 2,6-Pyridinedicarboxaldehyde 20949-84-2, 2-Methylthiazole-4-  
 carboxaldehyde 49579-01-3 49579-08-0 199599-68-3 199656-42-3  
 199656-43-4

RL: RCT (Reactant)

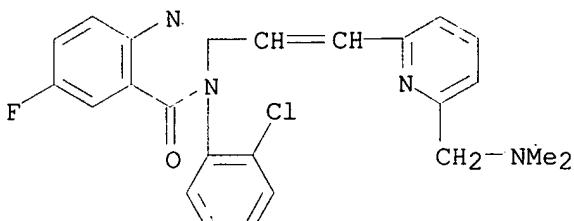
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT 38520-78-4P 49579-12-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT 199655-81-7P  
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

RN 199655-81-7 HCPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> fil uspatfull

FILE 'USPATFULL' ENTERED AT 16:45:05 ON 30 APR 2001  
 CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 24 Apr 2001 (20010424/PD)

FILE LAST UPDATED: 24 Apr 2001 (20010424/ED)

HIGHEST PATENT NUMBER: US6223348

CA INDEXING IS CURRENT THROUGH 24 Apr 2001 (20010424/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 24 Apr 2001 (20010424/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2000

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2000

>>> Page images are available for patents from 1/1/1997. Current <<<  
 >>> week patent text is typically loaded by Thursday morning and <<<  
 >>> page images are available for display by the end of the day. <<<  
 >>> Image data for the /FA field are available the following week. <<<

>>> Complete CA file indexing for chemical patents (or equivalents) <<<  
 >>> is included in file records. A thesaurus is available for the <<<  
 >>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL <<<  
 >>> fields. This thesaurus includes catchword terms from the <<<  
 >>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<  
 >>> available for the WIPO International Patent Classification <<<

>>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<<  
 >>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<<  
 >>> the /IC5 and /IC fields include the corresponding catchword <<<  
 >>> terms from the IPC subject headings and subheadings. <<<

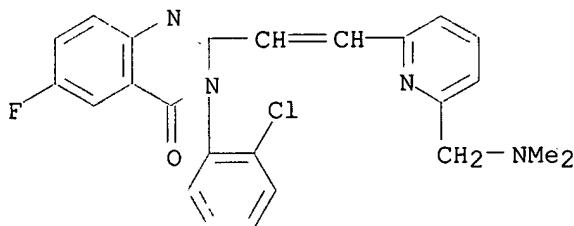
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitstr 190

L90 ANSWER 1 OF 1 USPATFULL  
 AN 2000:142378 USPATFULL  
 TI Methods of administering AMPA receptor antagonists to treat dyskinesias associated with dopamine agonist therapy  
 IN Chenard, Bertrand L., Waterford, CT, United States  
     Welch, Willard M., Mystic, CT, United States  
     Menniti, Frank S., Mystic, CT, United States  
 PA Pfizer Inc, New York, NY, United States (U.S. corporation)  
 PI US 6136812 20001024  
 AI US 1998-148974 19980904 (9)  
 PRAI US 1997-58098 19970905 (60)  
 DT Utility  
 EXNAM Primary Examiner: Jarvis, William R. A.  
 LREP Richardson, Peter C.; Ginsberg, Paul H.; Konstas, Kristina L.  
 CLMN Number of Claims: 10  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 2016  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB The invention relates to a method of treating dyskinesias associated with dopamine agonist therapy in a mammal which comprises administering to said mammal a compound, as defined herein, which is an antagonist of the AMPA receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 199655-81-7  
     (AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)  
 RN 199655-81-7 USPATFULL  
 CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> fil reg

FILE 'REGISTRY' ENTERED AT 16:45:26 ON 30 APR 2001  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2001 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 29 APR 2001 HIGHEST RN 333381-38-7  
 DICTIONARY FILE UPDATES: 29 APR 2001 HIGHEST RN 333381-38-7

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

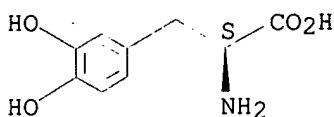
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d ide can 114

L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
 RN 59-92-7 REGISTRY  
 CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Alanine, 3-(3,4-dihydroxyphenyl)-, L- (8CI)  
 OTHER NAMES:  
 CN (-)-3,4-Dihydroxyphenylalanine  
 CN (-)-Dopa  
 CN .beta.-(3,4-Dihydroxyphenyl)-.alpha.-L-alanine  
 CN .beta.-(3,4-Dihydroxyphenyl)-L-alanine  
 CN .beta.-(3,4-Dihydroxyphenyl)alanine  
 CN 3,4-Dihydroxy-L-phenylalanine  
 CN 3,4-Dihydroxyphenyl-L-alanine  
 CN 3,4-Dihydroxyphenylalanine  
 CN 3-(3,4-Dihydroxyphenyl)-L-alanine  
 CN 3-Hydroxy-L-tyrosine  
 CN DA  
 CN Dihydroxy-L-phenylalanine  
 CN DOPA  
 CN Dopaflex  
 CN Dopalina  
 CN Dopar  
 CN Dopaston  
 CN Dopaston SE  
 CN Eldopal  
 CN Helfo-dopa  
 CN Insulamina  
 CN L-(-)-Dopa  
 CN L-.beta.-(3,4-Dihydroxyphenyl)-.alpha.-alanine  
 CN L-3-(3,4-Dihydroxyphenyl)alanine  
 CN L-4,5-Dihydroxyphenylalanine  
 CN L-DOPA  
 CN Larodopa  
 CN Levodopa  
 CN Levopa  
 CN Pardopa  
 FS STEREOSEARCH  
 DR 25525-15-9, 23734-74-9, 72572-99-7, 72573-00-3, 90638-38-3, 88250-23-1,  
 34241-25-3  
 MF C9 H11 N 04  
 CI COM  
 LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
 BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,  
 CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU,  
 EMBASE, GMELIN\*, HODOC\*, HSDB\*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,  
 MRCK\*, NAPRALERT, NIOSHTIC, PROMT, RTECS\*, SPECINFO, SYNTHLINE, TOXLINE,  
 TOXLIT, USAN, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, NDSL\*\*, TSCA\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



9109 REFERENCES IN FILE CA (1967 TO DATE)  
 260 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 9123 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

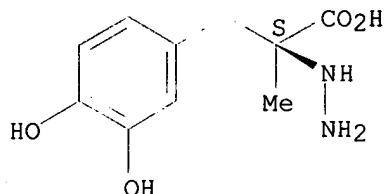
REFERENCE 1: 134:265967  
 REFERENCE 2: 134:265203  
 REFERENCE 3: 134:262181  
 REFERENCE 4: 134:261267  
 REFERENCE 5: 134:261182  
 REFERENCE 6: 134:251260  
 REFERENCE 7: 134:249755  
 REFERENCE 8: 134:249215  
 REFERENCE 9: 134:247378  
 REFERENCE 10: 134:242762

=> d ide can 117

L17 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
 RN 28860-95-9 REGISTRY  
 CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-,  
 (.alpha.S)- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-,  
 (S)-  
 CN Hydrocinnamic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, L-  
 (8CI)  
 OTHER NAMES:  
 CN (-)-L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylhydrocinnamic acid  
 CN (-)-L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylhydrocinnamic acid  
 monohydrate  
 CN .alpha.-Hydrazino-.alpha.-methyl-.beta.-(3,4-dihydroxyphenyl)propionic  
 acid  
 CN .alpha.-Methyldopahydrazine  
 CN 1-.alpha.-(3,4-Dihydroxybenzyl)-.alpha.-hydrazinopropionic acid  
 CN Carbidopa  
 CN Hydrazino-.alpha.-methyldopa  
 CN L-.alpha.-(3,4-Dihydroxybenzyl)-.alpha.-hydrazinopropionic acid  
 CN L-.alpha.-Hydrazino-.alpha.-methyl-.beta.-(3,4-dihydroxyphenyl)propionic  
 acid  
 CN L-.alpha.-Hydrazino-.alpha.-methyl-3,4-dihydroxyphenylpropionic acid  
 CN L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid  
 CN L-.alpha.-Methyl-.alpha.-hydrazino-.beta.-(3,4-dihydroxyphenyl)propionic  
 acid  
 CN L-.alpha.-Methyl-.alpha.-hydrazino-3,4-dihydroxyphenylpropionic acid  
 CN L-.alpha.-Methyl-.beta.-(3,4-dihydroxyphenyl)-.alpha.-hydrazinopropionic  
 acid  
 CN L-.alpha.-Methyldopahydrazine  
 CN L-3-(3,4-Dihydroxyphenyl)-2-methyl-2-hydrazinopropionic acid

CN MK 486  
 CN N-Aminomethyldopa  
 FS STEREOSEARCH  
 DR 27925-91-3, 31823-41-3  
 MF C10 H14 N2 O4  
 CI COM  
 LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
     BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN,  
     CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MRCK\*,  
     NIOSHTIC, PROMT, RTECS\*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL  
     (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, WHO  
     (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



540 REFERENCES IN FILE CA (1967 TO DATE)  
 7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 541 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:256873  
 REFERENCE 2: 134:242762  
 REFERENCE 3: 134:198100  
 REFERENCE 4: 134:188216  
 REFERENCE 5: 134:172697  
 REFERENCE 6: 134:168355  
 REFERENCE 7: 134:157584  
 REFERENCE 8: 134:157063  
 REFERENCE 9: 134:121022  
 REFERENCE 10: 134:120931

=> d ide can 120

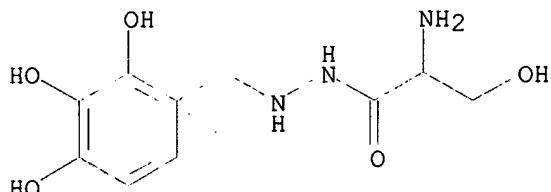
L20 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
 RN 322-35-0 REGISTRY  
 CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN DL-Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide  
 CN Serine, 2-(2,3,4-trihydroxybenzyl)hydrazide (7CI)  
 CN Serine, 2-(2,3,4-trihydroxybenzyl)hydrazide, DL- (8CI)  
 OTHER NAMES:  
 CN Benserazide  
 CN DL-Seryltrihydroxybenzylhydrazine  
 CN N-(DL-Seryl)-N'-(2,3,4-trihydroxybenzyl)hydrazine  
 CN N1-(DL-Seryl)-N2-(2,3,4-trihydroxybenzyl)hydrazine  
 CN N1-(DL-Seryl)-N2-(2,3,4-trihydroxybenzyl)hydrazine hydrochloride  
 CN Serazide

MF C10 H15 N3 O5

CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, NIOSHTIC, PROMT, RTECS\*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL  
 (\*File contains numerically searchable property data)

Other Sources: WHO



346 REFERENCES IN FILE CA (1967 TO DATE)

5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

347 REFERENCES IN FILE CAPLUS (1967 TO DATE)

20 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:249866

REFERENCE 2: 134:188216

REFERENCE 3: 134:105933

REFERENCE 4: 134:95504

REFERENCE 5: 134:3509

REFERENCE 6: 133:325730

REFERENCE 7: 133:256811

REFERENCE 8: 133:227909

REFERENCE 9: 133:183136

REFERENCE 10: 133:182991

=&gt; d ide can 140 tot

L40 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS

RN 57308-51-7 REGISTRY

CN L-Tyrosine, 3-hydroxy-, mixt. with (.alpha.S)-.alpha.-hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (S)-, mixt. contg.

CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)-, mixt. contg. (9CI)

CN L-Tyrosine, 3-hydroxy-, mixt. with (S)-.alpha.-hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid

OTHER NAMES:

CN Carbidopa-L-dopa mixt.

CN Carbidopa-levodopa mixt.

CN Isicom

CN Nacom

CN Nakom

CN Sinemet

FS STEREOSEARCH

MF C10 H14 N2 O4 . C9 H11 N O4

CI MXS

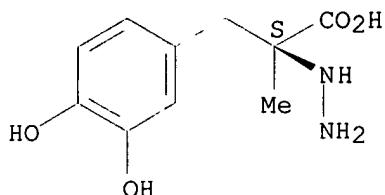
LC STN Files: BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CIN, DIOGENES, EMBASE, IMSDIRECTORY, MEDLINE, MRCK\*, PROMT, RTECS\*, TOXLINE, TOXLIT, USPATFULL  
(\*File contains numerically searchable property data)

CM 1

CRN 28860-95-9

CMF C10 H14 N2 O4

Absolute stereochemistry.

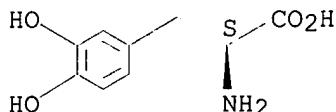


CM 2

CRN 59-92-7

CMF C9 H11 N O4

Absolute stereochemistry.



76 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

76 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:294727

REFERENCE 2: 133:204797

REFERENCE 3: 133:8986

REFERENCE 4: 131:165329

REFERENCE 5: 130:320759

REFERENCE 6: 130:261969

REFERENCE 7: 129:339741

REFERENCE 8: 129:301201

REFERENCE 9: 129:38404

REFERENCE 10: 128:212698

L40 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS

RN 37270-69-2 REGISTRY

CN L-Tyrosine, 3-hydroxy-, mixt. with serine 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN DL-Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide, mixt. contg.

CN L-Tyrosine, 3-hydroxy-, mixt. with DL-serine 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide

CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide, mixt. contg. (9CI)

OTHER NAMES:

CN Madopar

CN Ro 8-0576

FS STEREOSEARCH

DR 61949-25-5

MF C10 H15 N3 O5 . C9 H11 N O4

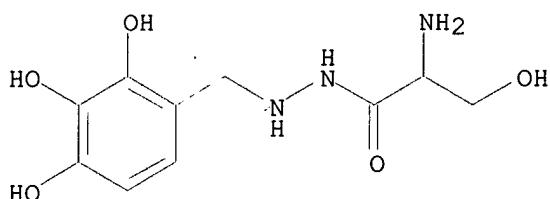
CI MXS

LC STN Files: BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, EMBASE, IMSDIRECTORY, MEDLINE, MRCK\*, PROMT, TOXLINE, TOXLIT, USPATFULL  
(\*File contains numerically searchable property data)

CM 1

CRN 322-35-0

CMF C10 H15 N3 O5

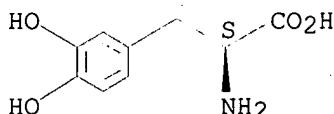


CM 2

CRN 59-92-7

CMF C9 H11 N O4

Absolute stereochemistry.



33 REFERENCES IN FILE CA (1967 TO DATE)

33 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:294727

REFERENCE 2: 131:266533

REFERENCE 3: 130:7366

REFERENCE 4: 129:239731

REFERENCE 5: 127:272715

REFERENCE 6: 124:250675

REFERENCE 7: 123:275785

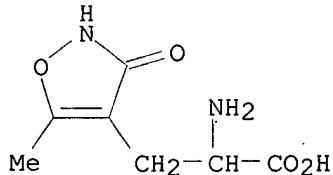
REFERENCE 8: 123:74239

REFERENCE 9: 123:782

REFERENCE 10: 122:96274

=> d ide can 19

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
 RN 77521-29-0 REGISTRY  
 CN 4-Isoxazolepropanoic acid, .alpha.-amino-2,3-dihydro-5-methyl-3-oxo- (9CI)  
 (CA INDEX NAME)  
 OTHER NAMES:  
 CN (.+-).-alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid  
 CN (R,S)-.alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid  
 CN (RS)-.alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid  
 CN .alpha.-Amino-2,3-dihydro-5-methyl-3-oxoisoxazole-4-propionic acid  
 CN .alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionate  
 CN .alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid  
 CN .gamma.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid  
 CN AMPA  
 CN AMPA (pharmaceutical)  
 CN D,L-.alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid  
 CN dl-.alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid  
 FS 3D CONCORD  
 DR 126632-03-9, 133481-32-0, 139261-99-7, 139559-02-7, 74341-63-2,  
 78729-80-3, 79697-77-1, 85506-19-0, 86495-63-8, 83354-19-2, 81323-87-7,  
 92614-50-1, 110592-37-5  
 MF C7 H10 N2 O4  
 CI COM  
 LC STN Files: BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT,  
 CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE,  
 MEDLINE, TOXLINE, TOXLIT, USPATFULL  
 (\*File contains numerically searchable property data)



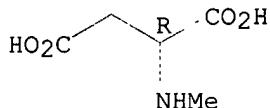
982 REFERENCES IN FILE CA (1967 TO DATE)  
 8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 982 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE	1:	134:264542
REFERENCE	2:	134:264541
REFERENCE	3:	134:202979
REFERENCE	4:	134:202883
REFERENCE	5:	134:190909
REFERENCE	6:	134:174165
REFERENCE	7:	134:173334
REFERENCE	8:	134:159650
REFERENCE	9:	134:158014
REFERENCE	10:	134:158002

=> d ide can 176 tot

L76 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS  
 RN 6384-92-5 REGISTRY  
 CN D-Aspartic acid, N-methyl- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Aspartic acid, N-methyl-, D- (8CI)  
 OTHER NAMES:  
 CN N-Methyl-D-aspartic acid  
 CN NMDA  
 FS STEREOSEARCH  
 MF C5 H9 N O4  
 CI COM  
 LC STN Files: AGRICOLA, AIDSLINE, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
 BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX,  
 CHEMLIST, CIN, CSCHEM, EMBASE, IFICDB, IFIUDB, IPA, MEDLINE, MRCK\*,  
 NIOSHTIC, PROMT, RTECS\*, TOXLINE, TOXLIT, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



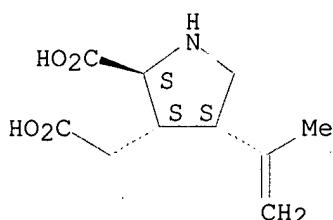
5598 REFERENCES IN FILE CA (1967 TO DATE)  
 9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 5603 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:264535  
 REFERENCE 2: 134:264523  
 REFERENCE 3: 134:264120  
 REFERENCE 4: 134:248974  
 REFERENCE 5: 134:247465  
 REFERENCE 6: 134:247458  
 REFERENCE 7: 134:232180  
 REFERENCE 8: 134:232146  
 REFERENCE 9: 134:232134  
 REFERENCE 10: 134:232120

L76 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS  
 RN 487-79-6 REGISTRY  
 CN 3-Pyrrolidineacetic acid, 2-carboxy-4-(1-methylethenyl)-, (2S,3S,4S)-  
 (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 3-Pyrrolidineacetic acid, 2-carboxy-4-(1-methylethenyl)-,  
 [2S-(2.alpha.,3.beta.,4.beta.)]-  
 CN 3-Pyrrolidineacetic acid, 2-carboxy-4-isopropenyl- (6CI, 7CI, 8CI)  
 OTHER NAMES:  
 CN (-)-.alpha.-Kainic acid  
 CN (-)-Kainic acid  
 CN (2S,3S,4S)-2-Carboxy-4-isopropenylpyrrolidine-3-acetic acid  
 CN .alpha.-Kainic acid

CN Digenic acid  
 CN Digenin  
 CN Helminal  
 CN Kainic acid  
 CN L.-alpha.-Kainic acid  
 FS STEREOSEARCH  
 DR 4071-38-9, 46398-96-3  
 MF C10 H15 N O4  
 CI COM  
 LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
     BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,  
     CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC\*, IPA,  
     MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PROMT, RTECS\*, SPECINFO,  
     TOXLINE, TOXLIT, USAN, USPATFULL, VETU  
     (\*File contains numerically searchable property data)  
 Other Sources: WHO

Absolute stereochemistry. Rotation (-).

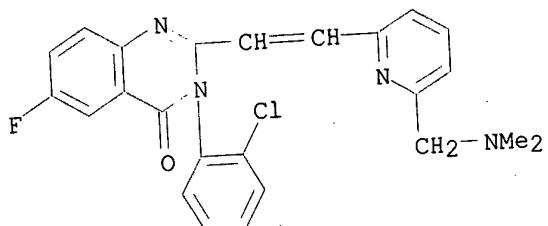


3858 REFERENCES IN FILE CA (1967 TO DATE)  
 41 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 3863 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 26 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:264545  
 REFERENCE 2: 134:261996  
 REFERENCE 3: 134:235967  
 REFERENCE 4: 134:232143  
 REFERENCE 5: 134:232142  
 REFERENCE 6: 134:232141  
 REFERENCE 7: 134:232100  
 REFERENCE 8: 134:222008  
 REFERENCE 9: 134:220893  
 REFERENCE 10: 134:218095

=> d ide can 125

L25 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
 RN 199655-81-7 REGISTRY  
 CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C24 H20 Cl F N4 O  
 CI COM  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



4 REFERENCES IN FILE CA (1967 TO DATE)  
 4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:218317

REFERENCE 2: 130:209717

REFERENCE 3: 129:230733

REFERENCE 4: 128:34774

=> d ide can 126

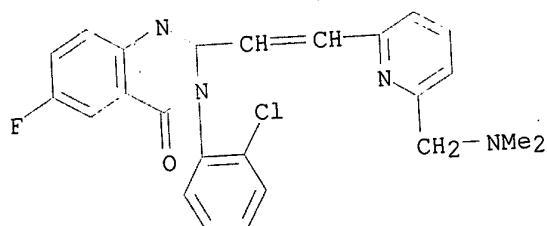
L26 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 220931-86-2 REGISTRY  
 CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX  
 NAME)

FS STEREOSEARCH  
 MF C24 H20 Cl F N4 O . C4 H4 O4  
 SR CA  
 LC STN Files: CA, CAPLUS

CM 1

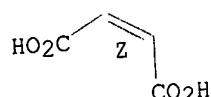
CRN 199655-81-7  
 CMF C24 H20 Cl F N4 O



CM 2

CRN 110-16-7  
 CMF C4 H4 O4

Double bond geometry as shown.



1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:209717

=> fil embase

FILE 'EMBASE' ENTERED AT 16:57:13 ON 30 APR 2001  
 COPYRIGHT (C) 2001 Elsevier Science B.V. All rights reserved.

FILE COVERS 1974 TO 19 Apr 2001 (20010419/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his 191-

(FILE 'HCAPLUS' ENTERED AT 16:44:40 ON 30 APR 2001)

FILE 'USPATFULL' ENTERED AT 16:45:05 ON 30 APR 2001

FILE 'REGISTRY' ENTERED AT 16:45:26 ON 30 APR 2001

FILE 'EMBASE' ENTERED AT 16:48:07 ON 30 APR 2001

L91 2635 S L9  
 L92 2635 S ALPHA AMINO 3 HYDROXY 5 METHYL 4 ISOXAZOLEPROPIONIC ACID/CT  
 L93 5086 S L91,L92 OR AMPA  
 L94 0 S L25 OR L26  
 L95 2291 S L40  
 L96 1807 S CARBIDOPA PLUS LEVODOPA/CT  
 L97 928 S BENSERAZIDE PLUS LEVODOPA/CT  
 L98 1679 S SINEMET OR MADOPAR  
 L99 3 S L93 AND L95-L98  
 L100 19733 S L14-L16  
 L101 1913 S LEVODOPA(L)CB/CT  
 L102 3422 S L17-L19  
 L103 951 S CARBIDOPA(L)CB/CT  
 L104 2216 S L20,L24  
 L105 472 S BENSERAZIDE(L)CB/CT  
 L106 1178 S L101 AND L103,L105  
 L107 3 S L106 AND L93  
 L108 6 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE  
 L109 7 S L99,L107,L108  
     E AMPA RECEPTOR ANTAGONIST/CT  
     E E3+ALL  
 L110 5732 S E5+NT  
 L111 33 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE  
 L112 9 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE  
 L113 10 S L109,L112

FILE 'EMBASE' ENTERED AT 16:57:13 ON 30 APR 2001

=> d all tot 1113

L113 ANSWER 1 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.  
 AN 2000150429 EMBASE

TI AMPA receptor blockade improves levodopa-induced dyskinesia in MPTP monkeys.

AU Konitsiotis S.; Blanchet P.J.; Verhagen L.; Lamers E.; Chase T.N.

CS Dr. T.N. Chase, Experimental Therapeutics Branch, Building 10, Natl. Inst. Neurol. Disorders/Stroke, Bethesda, MD 20892-1406, United States.  
 chase@helix.nih.gov

SO Neurology, (2000) 54/8 (1589-1595).

Refs: 49

ISSN: 0028-3878 CODEN: NEURAI  
 CY United States  
 DT Journal; Article  
 FS 008 Neurology and Neurosurgery  
 037 Drug Literature Index  
 LA English  
 SL English  
 AB Objective: To evaluate the contribution of amino-3-hydroxy-5-methyl-4-  
 isoxazole propionic acid (**AMPA**) glutamate receptors to the  
 pathogenesis of parkinsonian signs and levodopa-induced dyskinesias.  
 Background: Motor fluctuations and dyskinesias reflect, in part, altered  
 function of glutamate receptors of the NMDA subtype. The possible role of  
**AMPA** receptors, however, has not yet been examined. Methods: The  
 authors compared the ability of an **AMPA** agonist (CX516) and a  
 noncompetitive **AMPA** antagonist (LY300164) to alter parkinsonian  
 symptoms and levodopa-induced dyskinesia in MPTP-lesioned monkeys. Eight  
 levodopa-treated parkinsonian monkeys received rising doses of each drug,  
 first in monotherapy and then in combination with low-, medium-, and  
 high-dose levodopa. Results: CX516 alone, as well as when combined with  
 low-dose levodopa, did not affect motor activity but induced dyskinesia.  
 Moreover, following injection of the higher doses of levodopa, it  
 increased levodopa-induced dyskinesia by up to 52% ( $p < 0.05$ ). LY300164  
 potentiated the motor activating effects of low-dose levodopa, increasing  
 motor activity by as much as 86% ( $p < 0.05$ ), and that of medium-dose  
 levodopa as much as 54% ( $p < 0.05$ ). At the same time, LY300164 decreased  
 levodopa-induced dyskinesia by up to 40% ( $p < 0.05$ ). Conclusions:  
**AMPA** receptor upregulation may contribute to the expression of  
 levodopa-induced dyskinesia. Conceivably, noncompetitive **AMPA**  
 receptor antagonists could be useful, alone or in combination with NMDA  
 antagonists, in the treatment of PD, by enhancing the antiparkinsonian  
 effects of levodopa without increasing and possibly even decreasing  
 levodopa-induced dyskinesia.  
 CT Medical Descriptors:  
 \*dyskinesia: PC, prevention  
 \*Parkinson disease: PC, prevention  
 pathogenesis  
 monkey  
 dose response  
 receptor upregulation  
 receptor blocking  
 combination chemotherapy  
 disease severity  
 nonhuman  
 male  
 female  
 animal model  
 controlled study  
 animal tissue  
 animal cell  
 article  
 priority journal  
 Drug Descriptors:  
 \***AMPA** receptor agonist: PD, pharmacology  
 \***AMPA** receptor agonist: SC, subcutaneous drug administration  
 \***AMPA** receptor antagonist: CB, drug combination  
 \***AMPA** receptor antagonist: PD, pharmacology  
 \***AMPA** receptor antagonist: SC, subcutaneous drug administration  
 \*levodopa: PD, pharmacology  
 \*n methyl dextro aspartic acid receptor blocking agent: CB, drug  
 combination  
 \*n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology  
 6 quinoxalinecarboxylic acid piperide: PD, pharmacology  
 talampanel: PD, pharmacology  
 benserazide: PD, pharmacology  
 RN (levodopa) 59-92-7; (6 quinoxalinecarboxylic acid piperide)  
 154235-83-3; (talampanel) 161832-65-1, 161832-67-3; (benserazide)

14919-77-8, 322-35-0  
 CN (1) Cx 516; (2) Ly 300164  
 CO (1) Cortex (United States); (2) Lilly (United States); Research  
 Biochemicals

L113 ANSWER 2 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.  
 AN 96027659 EMBASE  
 DN 1996027659  
 TI Some central effects of GYKI 52466, a non-competitive **AMPA**  
 receptor antagonist.  
 AU Maj J.; Rogoz Z.; Skuza G.; Kolodziejczyk K.  
 CS Institute of Pharmacology, Polish Academy of Sciences, Smetna 12, 31-343  
 Krakow, Poland  
 SO Polish Journal of Pharmacology, (1995) 47/6 (501-507).  
 ISSN: 1230-6002 CODEN: PJPAE3  
 CY Poland  
 DT Journal; Article  
 FS 008 Neurology and Neurosurgery  
 030 Pharmacology  
 037 Drug Literature Index  
 LA English  
 SL English  
 AB GYKI 52466 [1-(4-aminophenyl)-4-methyl-7,8-methylenedioxy-5H-2,3-  
 benzodiazepine] has been described as a non-competitive **AMPA**  
 (non-NMDA glutamate) receptor antagonist. In the present paper some  
 behavioral effects of GYKI 52466 were studied in male Wistar rats and male  
 Albino Swiss mice. GYKI 52466 reduced the locomotor activity in normal  
 rats and mice, without evoking any symptoms of behavioral stimulation. The  
 CGP 37849-induced hyperlocomotion was increased by GYKI 52466. The  
 akinesia in monoamine-depleted rats was not affected by the drug studied.  
 The antiakinetic effect of L-DOPA was not changed by GYKI 52466, whereas  
 the antiakinetic effect of L-DOPA + CGP 37849 was decreased. GYKI 52466  
 increased the hyperlocomotion induced by apomorphine or cocaine. The drug  
 did not change the catalepsy induced by haloperidol or fluphenazine, as  
 well as the anticonvulsive effect of CGP 37849. GYKI 52466 was inactive in  
 the forced swimming test, but increased the antidepressant effect of CGP  
 37849. The flexor and extensor muscle tone of the rats hind limb was not  
 modified by GYKI 52466. The results obtained indicate that GYKI 52466  
 shows a neuropharmacological profile similar but not identical with that  
 of the quinoxalines (competitive **AMPA** receptor antagonists)  
 studied previously.  
 CT Medical Descriptors:  
 \*behavior  
 \*central nervous system  
 akinesia  
 animal experiment  
 article  
 catalepsy  
 controlled study  
 drug antagonism  
 drug potentiation  
 extensor muscle  
 flexor muscle  
 forced swimming test  
 hyperactivity  
 intraperitoneal drug administration  
 locomotion  
 male  
 monoamine metabolism  
 mouse  
 muscle tone  
 nonhuman  
 rat  
 subcutaneous drug administration  
 Drug Descriptors:  
 \* 1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine:

## IT, drug interaction

\*1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine:

## PD, pharmacology

\*quisqualic acid receptor: EC, endogenous compound

2 amino 4 methyl 5 phosphono 3 pentenoic acid: IT, drug interaction

2 amino 4 methyl 5 phosphono 3 pentenoic acid: CB, drug combination

2 amino 4 methyl 5 phosphono 3 pentenoic acid: PD, pharmacology

ampm receptor antagonist: PD, pharmacology

ampm receptor antagonist: IT, drug interaction

antidepressant agent: IT, drug interaction

antidepressant agent: PD, pharmacology

antidepressant agent: CB, drug combination

apomorphine: PD, pharmacology

apomorphine: IT, drug interaction

benserazide: PD, pharmacology

cocaine: IT, drug interaction

cocaine: PD, pharmacology

fluphenazine: PD, pharmacology

fluphenazine decanoate

glutamic acid antagonist: PD, pharmacology

glutamic acid antagonist: IT, drug interaction

haloperidol: PD, pharmacology

levodopa: IT, drug interaction

levodopa: PD, pharmacology

levodopa: CB, drug combination

metirosine: PD, pharmacology

quinoxaline derivative: PD, pharmacology

quinoxaline derivative: IT, drug interaction

reserpine: PD, pharmacology

RN (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine)  
 102771-26-6; (2 amino 4 methyl 5 phosphono 3 pentenoic acid) 127910-31-0;  
 (apomorphine) 314-19-2, 58-00-4; (benserazide) 14919-77-8,  
 322-35-0; (cocaine) 50-36-2, 53-21-4, 5937-29-1; (fluphenazine)  
 146-56-5, 69-23-8; (fluphenazine decanoate) 5002-47-1; (haloperidol)  
 52-86-8; (levodopa) 59-92-7; (metirosine) 672-87-7; (reserpine)  
 50-55-5, 8001-95-4

CN (1) Ro 4 4602; (2) Cgp 37849; (3) Lyogen; (4) Rausedyl

CO (1) Hoffmann la roche (Switzerland); (2) Ciba geigy (Switzerland); (3) Byk  
 gulden (Germany); (4) Richter (Hungary); Sandoz (Switzerland); Merck  
 (Germany); Reanal (Hungary); Institute for drug research (Hungary); Sigma  
 (United States)

L113 ANSWER 3 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 95309948 EMBASE

DN 1995309948

TI Some behavioral effects of CNQX and NBQX, AMPA receptor  
 antagonists.

AU Maj J.; Rogoz Z.; Skuza G.; Jaros T.

CS Institute of Pharmacology, Polish Academy of Sciences, Smetna 12,31-343  
 Krakow, Poland

SO Polish Journal of Pharmacology, (1995) 47/4 (269-277).  
 ISSN: 1230-6002 CODEN: PJPAE3

CY Poland

DT Journal; Article

FS 008 Neurology and Neurosurgery

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB CNQX (6-cyano-7-nitroquinoxaline-2,3-dione) and NBQX (2,3-dihydroxy-6-  
 nitro-7-sulfamoyl-benzo[f]quinoxaline), two competitive AMPA  
 (non-NMDA glutamate) receptor antagonists, as well as their interaction  
 with CGP 37849, a competitive NMDA receptor antagonist, were studied in  
 rats and mice. CNQX and NBQX inhibited the locomotor activity of naive  
 rats. No symptoms of behavioral excitation were observed. CGP 37849  
 induced locomotor hyperactivity which was reduced by CNQX and NBQX. In

monoamine-depleted rats (pretreated with reserpine + .alpha.-methyl-p-tyrosine), none of the two quinoxalines nor CGP 37849 antagonized akinesia. The antiakinetic effect of L-DOPA was increased by CGP 37849, but not by CNQX or NBQX. The latter action of CGP 37849 was decreased by CNQX and NBQX. The antiakinetic effect of clonidine was not changed by CNQX. The locomotor hyperactivity induced by apomorphine or cocaine was not modified by CNQX. Neither of the quinoxalines changed the catalepsy induced by haloperidol or spiperone. The fluphenazine catalepsy was slightly decreased by CNQX and increased by NBQX. CNQX and NBQX were inactive in the forced swimming test; CNQX (but not NBQX) increased the CGP 37849-induced reduction of the immobility time. CNQX decreased the muscle tone of hind limbs in naive and monoamine-depleted rats. The obtained results indicate that the **AMPA** receptor antagonists differ in their neuropharmacological profile from CGP 37849, an NMDA receptor antagonist. There is no positive cooperation (except for the forced swimming test) between NMDA and **AMPA** receptor antagonists; on the contrary, an antagonistic interaction between them has been observed.

## CT Medical Descriptors:

\*behavior  
akinesia  
animal experiment  
animal model  
article  
controlled study  
drug antagonism  
drug potentiation  
forced swimming test  
hyperactivity  
intraperitoneal drug administration  
locomotion  
male  
monoamine metabolism  
mouse  
muscle tone  
nonhuman  
rat  
subcutaneous drug administration

## Drug Descriptors:

\*quisqualic acid receptor  
\*2 amino 4 methyl 5 phosphono 3 pentenoic acid: IT, drug interaction  
\*2 amino 4 methyl 5 phosphono 3 pentenoic acid: PD, pharmacology  
\*6 cyano 7 nitro 2,3 quinoxalinedione: IT, drug interaction  
\*6 cyano 7 nitro 2,3 quinoxalinedione: PD, pharmacology  
\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD,  
pharmacology  
\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug  
interaction  
\*glutamic acid antagonist: PD, pharmacology  
\*glutamic acid antagonist: IT, drug interaction  
\*n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology  
\*n methyl dextro aspartic acid receptor blocking agent: IT, drug  
interaction  
ampa receptor antagonist: PD, pharmacology  
ampa receptor antagonist: IT, drug interaction  
apomorphine: PD, pharmacology  
benserazide: CB, drug combination  
benserazide: PD, pharmacology  
clonidine: PD, pharmacology  
cocaine: PD, pharmacology  
fluphenazine: PD, pharmacology  
fluphenazine: IT, drug interaction  
fluphenazine decanoate  
haloperidol: PD, pharmacology  
levodopa: CB, drug combination  
levodopa: IT, drug interaction

levodopa: PD, pharmacology  
 metirosine: PD, pharmacology  
 quinoxaline derivative: PD, pharmacology  
 quinoxaline derivative: IT, drug interaction  
 reserpine: PD, pharmacology  
 spiperone: PD, pharmacology  
 RN (2 amino 4 methyl 5 phosphono 3 pentenoic acid) 127910-31-0; (6 cyano 7  
 nitro 2,3 quinoxalinedione) 115066-14-3; (6 nitro 7  
 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (apomorphine)  
 314-19-2, 58-00-4; (benserazide) 14919-77-8, 322-35-0;  
 (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (cocaine) 50-36-2, 53-21-4,  
 5937-29-1; (fluphenazine) 146-56-5, 69-23-8; (fluphenazine decanoate)  
 5002-47-1; (haloperidol) 52-86-8; (levodopa) 59-92-7;  
 (metirosine) 672-87-7; (reserpine) 50-55-5, 8001-95-4; (spiperone)  
 749-02-0  
 CN (1) Cgp 37849; (2) Lyogen; (3) Rausedyl; (4) Ro 4 4602  
 CO (1) Ciba geigy (Switzerland); (2) Byk gulden (Germany); (3) Richter  
 (Hungary); (4) Hoffmann la roche (Switzerland); Sandoz (Switzerland); Rbi  
 (United States); Reanal (Hungary); Sigma (United States); Novo nordisk  
 (Denmark)

L113 ANSWER 4 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.  
 AN 95119361 EMBASE  
 DN 1995119361  
 TI Modulation of dopamine D1-mediated tuning behavior and striatal c-fos  
 expression by the substantia nigra.  
 AU Fenu S.; Carta A.; Morelli M.  
 CS Department of Toxicology, Viale A. Diaz 182, 09100 Cagliari, Italy  
 SO Synapse, (1995) 19/4 (233-240).  
 ISSN: 0887-4476 CODEN: SYNAET  
 CY United States  
 DT Journal; Article  
 FS 008 Neurology and Neurosurgery  
 030 Pharmacology  
 037 Drug Literature Index  
 052 Toxicology  
 LA English  
 SL English  
 AB In order to study the possible contribution of the substantia nigra (SN)  
 in the positive interaction between dopamine D1 receptor agonists and  
 glutamate antagonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned  
 rats, the effect of the D1 agonist, SKF 38393, was studied in combination  
 with intranigral infusions of glutamate antagonists of the NMDA (MK 801,  
 CPP) or AMPA (NBQX) type of receptor. Local infusion into the SN  
 of the 6-OHDA lesioned side of MK 801, CPP or NBQX at doses inducing no or  
 minimal behavioral effects significantly increased the turning behavior  
 and the expression of c-fos induced, in the lesioned caudate-putamen  
 (CPu), by a parenteral administration of SKF 38393. The same result was  
 obtained after intra-SN infusion of the GABA agonist, muscimol. High doses  
 of MK 801, CPP or muscimol infused into the SN produced intense  
 contralateral turning per se and induced a sparse c-fos expression in the  
 lesioned CPu which was antagonized by parenteral administration of MK 801.  
 The results indicate that a depression of SN pars reticulata efferent  
 neurons potentiates D1-mediated responses and suggest that this area may  
 play a role in the positive interaction between glutamate antagonists and  
 D1 receptor agonists.  
 CT Medical Descriptors:  
 \*substantia nigra  
 animal behavior  
 animal experiment  
 animal tissue  
 article  
 caudate nucleus  
 controlled study  
 drug infusion  
 gene expression

immunohistochemistry  
intracerebral drug administration  
intravenous drug administration

male

neuropharmacology

nonhuman

oncogene c fos

priority journal

putamen

rat

Drug Descriptors:

\*dopamine 1 receptor

n methyl dextro aspartic acid receptor

quisqualic acid receptor

\*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: CB, drug combination

\*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: PD, pharmacology

\*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: IT, drug interaction

\*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: DO, drug dose

\*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: CM, drug comparison

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CM, drug comparison

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug interaction

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose

\*dizocilpine: DO, drug dose

\*dizocilpine: IT, drug interaction

\*dizocilpine: PD, pharmacology

\*dizocilpine: CM, drug comparison

\*dizocilpine: CB, drug combination

\*dopamine 1 receptor blocking agent: DO, drug dose

\*dopamine 1 receptor blocking agent: IT, drug interaction

\*dopamine 1 receptor blocking agent: PD, pharmacology

\*dopamine 1 receptor blocking agent: CM, drug comparison

\*dopamine 1 receptor blocking agent: CB, drug combination

\*glutamic acid antagonist: IT, drug interaction

\*glutamic acid antagonist: DO, drug dose

\*glutamic acid antagonist: CM, drug comparison

\*glutamic acid antagonist: CB, drug combination

\*glutamic acid antagonist: PD, pharmacology

4 aminobutyric acid receptor stimulating agent: CB, drug combination

4 aminobutyric acid receptor stimulating agent: PD, pharmacology

4 aminobutyric acid receptor stimulating agent: IT, drug interaction

4 aminobutyric acid receptor stimulating agent: DO, drug dose

4 aminobutyric acid receptor stimulating agent: CM, drug comparison

benserazide

desipramine

levodopa

muscimol: DO, drug dose

muscimol: PD, pharmacology

muscimol: IT, drug interaction

muscimol: CB, drug combination

muscimol: CM, drug comparison

n methyl dextro aspartic acid receptor blocking agent: CM, drug comparison

n methyl dextro aspartic acid receptor blocking agent: CB, drug combination

n methyl dextro aspartic acid receptor blocking agent: IT, drug interaction

n methyl dextro aspartic acid receptor blocking agent: DO, drug dose

n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology  
 oxidopamine: TO, drug toxicity  
 RN (2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine) 67287-49-4;  
 (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7;  
 (dizocilpine) 77086-21-6; (benserazide) 14919-77-8, 322-35-0;  
 (desipramine) 50-47-5, 58-28-6; (levodopa) 59-92-7; (muscimol)  
 2763-96-4; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0  
 CN (1) Skf 38393; (2) Mk 801  
 CO (2) Rbi (United States); Hoffmann la roche (Switzerland); Ciba geigy  
 (Switzerland); Sigma (Italy); Novo nordisk (Denmark)

L113 ANSWER 5 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 94097346 EMBASE

DN 1994097346

TI Excitatory amino acid receptor antagonists modify regional cerebral metabolic responses to levodopa in 6-hydroxydopamine-lesioned rats.

AU Engber T.M.; Anderson J.J.; Boldry R.C.; Papa S.M.; Kuo S.; Chase T.N.

CS Experimental Therapeutics Branch, NINDS, Bethesda, MD 20892, United States

SO Neuroscience, (1994) 59/2 (389-399).

ISSN: 0306-4522 CODEN: NRSCDN

CY United Kingdom

DT Journal; Article

FS 002 Physiology

008 Neurology and Neurosurgery

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB Excitatory amino acid receptor antagonists have been proposed as novel therapeutic agents to be used with levodopa in the treatment of Parkinson's disease. We examined the neural substrates for the interaction between levodopa and antagonists of either the .alpha.-amino-3-hydroxy-5-methylisoxazole- 4-propionic acid or N-methyl-D-aspartate type of excitatory amino acid receptor using 2-deoxyglucose autoradiography. Thus, we compared the effects of the .alpha.-amino-3-hydroxy-5-methylisoxazole-4-propionic acid receptor antagonist 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(F)quinoxaline (10 mg/kg, i.v.) and the N-methyl-D-aspartate antagonist MK-801 (0.1 mg/kg, i.v.) on cerebral metabolic responses to levodopa (25 mg/kg, i.v. with 12.5 mg/kg benserazide) in rats with a unilateral nigrostriatal pathway lesion. Levodopa increased glucose utilization ipsilateral to the lesion in substantia nigra pars reticula (up to 104%), entopeduncular nucleus (up 90%) and subthalamic nucleus (up 30%), indicating that levodopa alters striatal output through the striatonigral, striatoentopeduncular and striatopallidal pathways. Levodopa also decreased metabolic rate in lateral habenula (down 39%), a target of projections from entopeduncular nucleus, implying a reduction in basal ganglia output. 2,3-Dihydroxy-6-nitro-7-sulfamoylbenzo(F)quinoxaline and MK- 801 by themselves did not affect glucose utilization in any of these regions. Pretreatment with 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(F)quinoxaline reduced the effect of levodopa in substantia nigra pars reticulata but not in entopeduncular nucleus or subthalamic nucleus, while MK-801 attenuated the effect of levodopa in all three of these structures; neither 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(F)quinoxaline nor MK-801 altered the effect of levodopa in lateral habenula. When given at the same doses to a separate group of lesioned animals, neither 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(F)quinoxaline nor MK-801 affected rotational behavior elicited by levodopa. These findings indicate that .alpha.-amino-3-hydroxy-5-methylisoxazole- 4-propionic acid and N-methyl-D-aspartate receptor antagonists differentially modify dopamine receptor-mediated striatal output. .alpha.-Amino-3-hydroxy-5- methylisoxazole-4-propionic acid receptor blockade may preferentially attenuate the effect of dopamine receptor activation on the striatonigral pathway, while N-methyl-D-aspartate blockade appears to reduce the actions of dopamine on the striatonigral, striatoentopeduncular and striatopallidal pathways. However, the lack of effect of both 2,3-dihydroxy-6-nitro-7-

sulfamoyl-benzo(F)quinoxaline and MK-801 on levodopa-induced rotational behavior and reduced metabolic rate in the lateral habenula suggests that neither .alpha.-amino-3-hydroxy-5-methylisoxazole-4-propionic acid nor N-methyl- D-aspartate receptor blockade diminishes the net effect of levodopa on basal ganglia output.

CT Medical Descriptors:

- \*nigroneostriatal system
- animal experiment
- animal model
- animal tissue
- article
- autoradiography
- brain region
- circling behavior
- controlled study
- intravenous drug administration
- male
- nonhuman
- parkinson disease: DT, drug therapy
- priority journal
- rat

Drug Descriptors:

- \*dopamine receptor
- \*glutamate receptor
- \*n methyl dextro aspartic acid receptor
- quisqualic acid receptor
  - \*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination
  - \*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CM, drug comparison
  - \*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug interaction
  - \*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology
- \*deoxyglucose
- \*dizocilpine: CB, drug combination
- \*dizocilpine: CM, drug comparison
- \*dizocilpine: IT, drug interaction
- \*dizocilpine: PD, pharmacology
- \*glutamic acid antagonist: PD, pharmacology
- \*glutamic acid antagonist: CB, drug combination
- \*glutamic acid antagonist: CM, drug comparison
- \*glutamic acid antagonist: IT, drug interaction
  - \*levodopa: IT, drug interaction
  - \*levodopa: PD, pharmacology
- \*oxidopamine: TO, drug toxicity
  - benserazide: CB, drug combination

RN (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7;  
 (deoxyglucose) 154-17-6; (dizocilpine) 77086-21-6; (levodopa)  
 59-92-7; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0;  
 (benserazide) 14919-77-8, 322-35-0

CN (1) Mk 801

CO (1) Rbi (United States); Sigma (United States); Novo nordisk (Denmark);  
 Hoffmann la roche (United States)

L113 ANSWER 6 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 94039675 EMBASE

DN 1994039675

TI The **AMPA** antagonists NBQX and GYKI 52466 do not counteract neuroleptic- induced catalepsy.

AU Zadow B.; Schmidt W.J.

CS Neuropharmacology Division, Zoological Institute, University of Tubingen,  
 Mohlstrasse 54/1, D-72074 Tubingen, Germany

SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1994) 349/1 (61-65).

CY ISSN: 0028-1298 CODEN: NSAPCC

Germany

DT Journal; Article  
 FS 008 Neurology and Neurosurgery  
 030 Pharmacology  
 037 Drug Literature Index  
 LA English  
 SL English  
 AB The **AMPA** antagonists NBQX (2.5, 5, 10 mg/kg) and GYKI 52466 (4.8, 8 mg/kg) were investigated in haloperidol (0.5 mg/kg)-induced catalepsy in the rat. The effects of **AMPA** antagonists administered either alone or in combination with the noncompetitive NMDA antagonist dizocilpine (0.02 mg/kg), with the dopamine D-2 agonist quinpirole (1 mg/kg) or with L-DOPA (50, 100 mg/kg plus benserazide) were tested. NBQX or GYKI 52466 did not exert anticataleptic effects, neither alone nor in combination with dizocilpine, quinpirole or L-DOPA. Thus, in the rat inhibition of **AMPA** receptors with NBQX or GYKI 52466 does not have effects predictive for an antiparkinsonian potential.  
 CT Medical Descriptors:  
 \*catalepsy  
 animal experiment  
 article  
 controlled study  
 intraperitoneal drug administration  
 male  
 nonhuman  
 oral drug administration  
 rat  
 Drug Descriptors:  
 \*excitatory amino acid receptor  
 quisqualic acid receptor  
 \*1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine:  
 PD, pharmacology  
 \*1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine:  
 DO, drug dose  
 \*1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine:  
 CB, drug combination  
 \*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose  
 \*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug  
 combination  
 \*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD,  
 pharmacology  
 \*amino acid receptor blocking agent: CB, drug combination  
 \*amino acid receptor blocking agent: DO, drug dose  
 \*amino acid receptor blocking agent: PD, pharmacology  
 \*benserazide: CB, drug combination  
 \*neuroleptic agent: PD, pharmacology  
 ampa receptor antagonist: CB, drug combination  
 ampa receptor antagonist: DO, drug dose  
 ampa receptor antagonist: PD, pharmacology  
 benserazide plus levodopa: PD, pharmacology  
 benserazide plus levodopa: CB, drug combination  
 dizocilpine: PD, pharmacology  
 dizocilpine: CB, drug combination  
 dopamine 2 receptor stimulating agent: CB, drug combination  
 dopamine 2 receptor stimulating agent: PD, pharmacology  
 levodopa: CB, drug combination  
 quinpirole: CB, drug combination  
 quinpirole: PD, pharmacology  
 RN (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine)  
 102771-26-6; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione)  
 118876-58-7; (benserazide) 14919-77-8, 322-35-0; (benserazide  
 plus levodopa) 37270-69-2; (dizocilpine) 77086-21-6; (levodopa)  
 59-92-7; (quinpirole) 73625-62-4, 80373-22-4, 85760-75-4,  
 85798-08-9  
 CN (1) Mk 801; (2) Madopar; (3) Gyki 52466  
 CO (1) Merck sharp and dohme (Germany); (2) Hoffmann la roche (Germany); (3)  
 Institute for drug research (Hungary); Novo nordisk (Denmark); Janssen

(Germany); Biotrend (Germany)

L113 ANSWER 7 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.  
AN 93131307 EMBASE  
DN 1993131307  
TI Glutamate-dopamine interactions in the basal ganglia: Relationship to Parkinson's disease.  
AU Greenamyre J.T.  
CS Department of Neurology, University of Rochester, 601 Elmwood Ave, Rochester, NY 14642, United States  
SO Journal of Neural Transmission - General Section, (1993) 91/2-3 (255-269). ISSN: 0300-9564 CODEN: JNTMAH  
CY Austria  
DT Journal; General Review  
FS 008 Neurology and Neurosurgery  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LA English  
SL English  
AB Current antiparkinsonian therapies focus on either replacing dopamine via precursor (L-DOPA) administration, or directly stimulating postsynaptic dopamine receptors with dopamine agonists. Unfortunately, this approach is associated with numerous side effects and these drugs lose efficacy with disease progression. This article reviews recent evidence which suggests that negative modulation of glutamatergic neurotransmission has antiparkinsonian effects in a variety of rodent and primate models of parkinsonism. The pronounced synergism between dopaminergic agents and glutamate receptor antagonists may provide a means of using very low doses of the two drug classes in concert to treat Parkinson's disease effectively and minimize dose-related drug side effects.  
CT Medical Descriptors:  
\*basal ganglion  
\*parkinson disease: ET, etiology  
\*parkinson disease: DT, drug therapy  
animal model  
disease course  
drug effect  
drug efficacy  
drug potentiation  
functional anatomy  
modulation  
neuroanatomy  
neurotransmission  
nonhuman  
primate  
priority journal  
review  
rodent  
side effect  
subthalamic nucleus  
Drug Descriptors:  
dopamine receptor  
n methyl dextro aspartic acid receptor  
\*dopamine: EC, endogenous compound  
\*glutamic acid: EC, endogenous compound  
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: PD, pharmacology  
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: DT, drug therapy  
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology  
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DT, drug therapy  
6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination  
carbidopa: PD, pharmacology  
carbidopa: CB, drug combination  
dopamine receptor stimulating agent: DT, drug therapy  
dopamine receptor stimulating agent: IT, drug interaction

dopamine receptor stimulating agent: DO, drug dose  
 dopamine receptor stimulating agent: CB, drug combination  
 dopamine receptor stimulating agent: AE, adverse drug reaction  
 glutamic acid antagonist: CB, drug combination  
 glutamic acid antagonist: DO, drug dose  
 glutamic acid antagonist: IT, drug interaction  
 glutamic acid antagonist: DT, drug therapy

levodopa: PD, pharmacology  
 levodopa: DT, drug therapy  
 levodopa: CB, drug combination  
 levodopa: AE, adverse drug reaction

RN (dopamine) 51-61-6, 62-31-7; (glutamic acid) 11070-68-1, 138-15-8,  
 56-86-0, 6899-05-4; (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine)  
 28289-54-5; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione)  
 118876-58-7; (carbidopa) 28860-95-9; (levodopa) 59-92-7

L113 ANSWER 8 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 93058820 EMBASE

DN 1993058820

TI Excitatory amino acid antagonists and Parkinson's disease.

AU Rosario Luquin M.; Martinez-Lage J.M.

CS Department Neurology/Neurosurgery, Clinica Universitaria, Medical  
 School, Pamplona, Spain

SO New Trends in Clinical Neuropharmacology, (1992) 6/1-4 (43-47).

ISSN: 0393-5345 CODEN: NTCNEP

CY Italy

DT Journal; Article

FS 008 Neurology and Neurosurgery

052 Toxicology

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB We have studied the motor response induced by the administration of the AMPA-antagonist NBQX given alone or simultaneously with l-dopa to 2 parkinsonian monkeys. NBQX (1, 2 and 4 mg/kg im) failed to reverse parkinsonism. Similarly, co-administration of NBQX (1 mg/kg) plus l-dopa (12.5, 25 and 50 mg orally) did not modify the motor improvement and dyskinesia induced by l-dopa. These results suggest that NBQX can not be considered as a useful treatment for Parkinson's disease.

CT Medical Descriptors:

\*motor dysfunction

\*parkinson disease: DT, drug therapy

animal experiment

animal model

article

controlled study

dyskinesia

intramuscular drug administration

monkey

nonhuman

oral drug administration

Drug Descriptors:

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug

combination

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DT, drug

therapy

\*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD,

pharmacology

\*amino acid receptor blocking agent: PD, pharmacology

\*amino acid receptor blocking agent: DT, drug therapy

\*amino acid receptor blocking agent: DO, drug dose

\*amino acid receptor blocking agent: CB, drug combination

\*levodopa: CB, drug combination

\*levodopa: DT, drug therapy

\*levodopa: PD, pharmacology  
 \*levodopa: TO, drug toxicity  
 \*levodopa: DO, drug dose

1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: TO, drug toxicity

benserazide: DT, drug therapy

benserazide: CB, drug combination

benserazide plus levodopa

naxagolide: DT, drug therapy

RN (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (levodopa) 59-92-7; (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (benserazide) 14919-77-8, 322-35-0; (benserazide plus levodopa) 37270-69-2; (naxagolide) 88058-88-2

CN (1) Madopar

CO (1) Hoffmann la roche; Novo nordisk

L113 ANSWER 9 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 91340439 EMBASE

DN 1991340439

TI The **AMPA** receptor antagonist NBQX has antiparkinsonian effects in monoamine-depleted rats and MPTP-treated monkeys.

AU Klockgether T.; Turski L.; Honore T.; Zhang Z.; Gash D.M.; Kurlan R.; Greenamyre J.T.

CS Department of Neurology, Rochester Univ. Medical Center, Box 673, 601 Elmwood Ave, Rochester, NY 14642, United States

SO Annals of Neurology, (1991) 30/5 (717-723).

ISSN: 0364-5134 CODEN: ANNED3

CY United States

DT Journal; Article

FS 008 Neurology and Neurosurgery

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB Abnormally increased subthalamic nucleus output to the internal pallidal segment and the reticular part of the substantia nigra plays a critical pathophysiological role in the development of parkinsonism. Because synaptic transmission of subthalamic output is glutamatergic and mediated, in part, by the .alpha.-amino-3-hydroxy-5-methyl-4-isoxazole propionate (**AMPA**) subtype of glutamate receptor, **AMPA** receptor antagonists may possess antiparkinsonian properties. We report that in monoamine-depleted rats, 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(f)quinoxaline (NBQX) (Novo-Nordisk, Copenhagen, Denmark)-a selective antagonist of the **AMPA** subtype of glutamate receptor-suppressed muscular rigidity but had no effect on akinesia. NBQX microinjected into the subthalamic nucleus, internal pallidal segment, and reticular part of the substantia nigra, but not into the laterodorsal neostriatum of the rats, stimulated locomotor activity and reduced muscular rigidity. In aged Rhesus monkeys with bilateral 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced parkinsonism, intramuscular NBQX produced clinically apparent improvement in akinesia, tremor, posture, and gross motor skills. NBQX also potentiated the antiparkinsonian effects of L-3,4-dihydroxyphenylalanine in both rats and monkeys. Blockade of excitatory synaptic transmission by **AMPA** receptor antagonists may provide a new therapeutic strategy for Parkinson's disease (PD).

CT Medical Descriptors:

\*parkinsonism

\*rigidity

animal model

article

female

intramuscular drug administration

male

monkey

nonhuman

priority journal

Drug Descriptors:

\*1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine  
 \*reserpine  
 6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione  
 carbidopa plus levodopa  
 RN (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (reserpine)  
 50-55-5, 8001-95-4; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione)  
 118876-58-7; (carbidopa plus levodopa) 57308-51-7  
 CN (1) Sinemet  
 CO (1) Merck sharp and dohme; Novo nordisk (Denmark)

L113 ANSWER 10 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.  
 AN 80251895 EMBASE  
 DN 1980251895  
 TI Kainic acid-induced wet dog shakes in rats. The relation to central  
 neurotransmitters.  
 AU Kleinrok Z.; Turski L.  
 CS Dept. Pharmacol., Inst. Clin. Pathol., Med. Sch., PL-20-090 Lublin, Poland  
 SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1980) 314/1 (37-46).  
 CODEN: NSAPCC  
 CY Germany  
 DT Journal  
 FS 030 Pharmacology  
 050 Epilepsy  
 037 Drug Literature Index  
 008 Neurology and Neurosurgery  
 LA English  
 AB Following the intracerebroventricular administration of kainic acid (KA),  
 rats showed wet dog shakes (WDS) in a dose-dependent manner.  
 DL-.alpha.-amino adipic acid and L-glutamic acid diethylester blocked WDS  
 behavior induced by 0.05 .mu.g of KA. Noradrenaline, clonidine, yohimbine  
 and apomorphine also significantly blocked KA-induced WDS. Phentolamine  
 and propranolol did not affect WDS. FLA 63, 6-OHDA lesion and bilateralis  
 electrolytic lesion to locus coeruleus markedly enhanced, but L-Dopa  
 blocked WDS behavior. Moreover, the KA-induced shaking behavior was  
 blocked by .alpha.-methyl-p-tyrosine and haloperidol. Cyproheptadine and  
 methergoline also blocked WDS. p-Chlorophenylalanine, 5,6-DHT lesion,  
 electrolytic lesions to dorsal and medial raphe nuclei showed no effect on  
 WDS behavior, but L-5-hydroxytryptophan efficiently blocked it. Atropine  
 and morphine considerably blocked KA-induced WDS behavior, but pilocarpine  
 and nalorphine showed no effect. Bicuculline significantly enhanced, but  
 aminooxyacetic acid blocked WDS. Intracerebroventricularly administered KA  
 dose-dependently decreased the concentrations of noradrenaline and  
 dopamine in the whole rat brain. The brain concentration of  
 5-hydroxytryptamine was unchanged. In contrast the concentration of  
 5-hydroxyindoleacetic acid increased. KA was ineffective regarding the  
 GABA concentration and GAD activity. KA dose-dependently accelerated the  
 disappearance of brain noradrenaline and dopamine after inhibition of  
 catecholamine synthesis. KA, following inhibition of monoamine oxidase,  
 increased the accumulation of 5-hydroxytryptamine, but failed to change  
 the rate of decline of 5-hydroxyindoleacetic acid. KA failed to change the  
 disappearance of brain 5-hydroxytryptamine after inhibition of its  
 synthesis by PCPA. It is suggested that KA-induced WDS behavior is  
 independent from the increased activity of serotonergic neurons in the  
 central nervous system. KA-induced WDS appears to be under the inhibitory  
 control of noradrenergic and GABA-ergic activity. The weaker inhibitory  
 effect upon this behavior showed also dopaminergic and serotonergic  
 neurons. The present experiments showed the close relationship between  
 KA-induced WDS and shaking behavior in morphine abstinence, but basic  
 differences in WDS behavior caused by excessive stimulation of  
 serotonergic receptors.  
 CT Medical Descriptors:  
 \*5,6 dihydroxytryptophan  
 \*brain injury  
 \*locus ceruleus  
 \*raphe nucleus  
 \*wet dog shakes

withdrawal syndrome  
 intracerebral drug administration  
 dose response  
 drug comparison  
 drug withdrawal  
 rat  
 drug response  
 therapy  
 central nervous system  
 animal experiment  
 intracerebroventricular drug administration  
 intraperitoneal drug administration  
 subcutaneous drug administration  
 Drug Descriptors:  
 \*4 aminobutyric acid  
 \*5 hydroxytryptophan  
 \*oxidopamine  
 \*amino adipic acid  
 \*apomorphine  
 \*atropine  
 \*benserazide  
 \*bis(4 methyl 1 homopiperazinylthiocarbonyl)disulfide  
 \*aminoxyacetic acid  
 \*clonidine  
 \*cyproheptadine  
 \*dopamine  
 \*fenclonine  
 \*glutamic acid diethyl ester  
 \*haloperidol  
 \*kainic acid  
 \*levodopa  
 \*metergoline  
 \*metirosine  
 \*morphine  
 \*nalorphine  
 \*neurotransmitter  
 \*noradrenalin  
 \*phentolamine  
 \*pilocarpine  
 \*serotonin  
 \*yohimbine  
 bicuculline  
 propranolol

RN (4 aminobutyric acid) 28805-76-7, 56-12-2; (5 hydroxytryptophan) 4350-09-8, 56-69-9; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0; (amino adipic acid) 52047-41-3; (apomorphine) 314-19-2, 58-00-4; (atropine) 51-55-8, 55-48-1; (benserazide) 14919-77-8, 322-35-0; (bis(4 methyl 1 homopiperazinylthiocarbonyl)disulfide) 26087-98-9; (aminoxyacetic acid) 2921-14-4, 645-88-5; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (cyproheptadine) 129-03-3, 969-33-5; (dopamine) 51-61-6, 62-31-7; (fenclonine) 1991-78-2, 7424-00-2; (glutamic acid diethyl ester) 16450-41-2; (haloperidol) 52-86-8; (kainic acid) 487-79-6; (levodopa) 59-92-7; (metergoline) 17692-51-2; (metirosine) 672-87-7; (morphine) 52-26-6, 57-27-2; (nalorphine) 1041-90-3, 57-29-4, 62-67-9; (noradrenalin) 1407-84-7, 51-41-2; (phentolamine) 50-60-2, 73-05-2; (pilocarpine) 148-72-1, 54-71-7, 92-13-7; (serotonin) 50-67-9; (yohimbine) 146-48-5, 65-19-0; (bicuculline) 485-49-4; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6

CN Fla 63; Ro 4 4602  
 CO Sigma (United States); Polfa (Poland); Sandoz (Luxembourg); Merck (Germany); Vacom (Yugoslavia); Koch light (United Kingdom); Ciba geigy (Switzerland); Chinoin (Hungary); Kistner (Sweden); Boehringer Ingelheim (Germany); Richter (Hungary); Roche (Switzerland)

FILE 'BIOSIS' ENTERED AT 17:04:57 ON 30 APR 2001  
 COPYRIGHT (C) 2001 BIOSIS(R)

FILE COVERS 1969 TO DATE.  
 CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT  
 FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 25 April 2001 (20010425/ED)

The BIOSIS file has been reloaded. Enter HELP RLOAD and HELP REINDEXING for details.

=> d all tot

L128 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS  
 AN 2001:147868 BIOSIS  
 DN PREV200100147868  
 TI Atropisomeric **quinazolin-4-one** derivatives are potent noncompetitive **alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)** receptor antagonists.  
 AU Welch, W. M.; Ewing, F. E.; Huang, J.; Menniti, F. S.; Pagnozzi, M. J.; Kelly, K.; Seymour, P. A.; Guanowsky, V.; Guhan, S.; Guinn, M. R.; Critchett, D.; Lazzaro, J.; Ganong, A. H.; DeVries, K. M.; Staigers, T. L.; Chenard, B. L. (1)  
 CS (1) Global Research and Development, Groton Laboratories, Pfizer Inc., Groton, CT, 06340: chenardbl@groton.pfizer.com USA  
 SO Bioorganic & Medicinal Chemistry Letters, (22 January, 2001) Vol. 11, No. 2, pp: 177-181. print.  
 ISSN: 0960-894X.  
 DT Article  
 LA English  
 SL English  
 AB Piriqualone (1) was found to be an antagonist of **AMPA** receptors. Structure-activity optimization was conducted on each of the three rings in 1 to afford a series of potent and selective antagonists. The sterically crowded environment surrounding the N-3 aryl group provided sufficient thermal stability for atropisomers to be isolated. Separation of these atropisomers resulted in the identification of (+)-38 (CP-465,022), a compound that binds to the **AMPA** receptor with high affinity (IC50=36nM) and displays potent anticonvulsant activity.  
 CC Pharmacology - Neuropharmacology \*22024  
 Biochemical Studies - General \*10060  
 Pathology, General and Miscellaneous - Therapy \*12512  
 Pharmacology - General \*22002  
 IT Major Concepts  
 Biochemistry and Molecular Biophysics; Pharmaceuticals (Pharmacology)  
 IT Chemicals & Biochemicals  
 CP-465,022: anticonvulsant - drug; **alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid** receptor; piriqualone: **alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid** receptor antagonist; **quinazolin-4-one**: **alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid** receptor antagonist, derivatives  
 RN 199655-36-2 (CP-465,022)  
 1897-89-8 (PIRIQUALONE)  
 491-36-1 (QUINAZOLIN-4-ONE)

L128 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS  
 AN 2001:45788 BIOSIS  
 DN PREV200100045788  
 TI Quinazoline-4-one **AMPA** antagonists.  
 AU Chenard, Bertrand L.; Welch, Willard M. (1)  
 CS (1) Mystic, CT USA  
 ASSIGNEE: Pfizer Inc

PI US 6060479 May 09, 2000  
 SO Official Gazette of the United States Patent and Trademark Office Patents,  
 (May 9, 2000) Vol. 1234, No. 2, pp. No Pagination. e-file.  
 ISSN: 0098-1133.

DT Patent

LA English

AB The present invention relates to novel **quinazolin-4-one** derivatives of the formula I, as defined in the specification, pharmaceutical compositions containing such compounds the use of such compounds to treat neurodegenerative, psychotropic, and drug and alcohol induced central and peripheral nervous system disorders.

NCL 514258000

IT Major Concepts

Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences); Pharmaceuticals (Pharmacology)

IT Diseases

nervous system disorders: alcohol-induced, drug-induced, nervous system disease; neurodegenerative disorders: nervous system disease; psychotropic disorder: behavioral and mental disorders, nervous system disease

IT Chemicals & Biochemicals

**quinazolin-4-one**: **AMPA** antagonist, derivatives, pharmaceutical

RN 491-36-1 (**QUINAZOLIN-4-ONE**)

L128 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS

AN 2000:355669 BIOSIS

DN PREV200000355669

TI Methaqualone derivatives are potent noncompetitive **AMPA** receptor antagonists.

AU Chenard, B. L. (1); Menniti, F. S.; Pagnozzi, M. J.;  
 Shenk, K. D.; Ewing, F. E.; Welch, W. M.

CS (1) Central Research Division, Pfizer Inc., Groton, CT, 06340 USA

SO Bioorganic & Medicinal Chemistry Letters, (5 June, 2000) Vol. 10, No. 11,  
 pp. 1203-1205. print.

ISSN: 0960-894X.

DT Article

LA English

SL English

AB **Quinazolin-4-one** derivatives of methaqualone substituted at C-2 define a new class of noncompetitive antagonists at **AMPA** receptors.

CC Biochemical Studies - General \*10060

Pathology, General and Miscellaneous - Therapy \*12512

Nervous System - Physiology and Biochemistry \*20504

Pharmacology - General \*22002

IT Major Concepts

Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination); Pharmacology

IT Parts, Structures, & Systems of Organisms

central nervous system: nervous system

IT Chemicals & Biochemicals

2-amino-3-(3-hydroxy-5-methyl-4-isoxazolyl)-propionate receptor; methaqualone derivative: anticonvulsant activity, noncompetitive 2-amino-3-(3-hydroxy-5-methyl-4-isoxazolyl)-propionate receptor antagonist, pyridine ring modification; **quinazolin-4-one**: synthesis

RN 491-36-1 (**QUINAZOLIN-4-ONE**)

L128 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS

AN 2000:222771 BIOSIS

DN PREV200000222771

TI Discovery of a potent and selective series of noncompetitive **quinazolinone AMPA** antagonists.

AU Welch, Willard M. (1); Huang, J. H. (1); Ewing, F. E. (1);

Menniti, F. S. (1); Pagnozzi, M. J. (1); Banker, M. J. (1);  
Devries, K. M. (1)  
CS (1) Department of Medicinal Chemistry, Pfizer Inc, Eastern Point Road,  
Groton, CT, 06340 USA  
SO Abstracts of Papers American Chemical Society, (2000) Vol. 219, No. 1-2,  
pp. MEDI 325.  
Meeting Info.: 219th Meeting of the American Chemical Society. San  
Francisco, California, USA March 26-30, 2000 American Chemical Society  
. ISSN: 0065-7727.  
DT Conference  
LA English  
SL English  
CC Pharmacology - General \*22002  
Cytology and Cytochemistry - General \*02502  
Biochemical Methods - General \*10050  
Biochemical Methods - Proteins, Peptides and Amino Acids \*10054  
Biochemical Studies - Proteins, Peptides and Amino Acids \*10064  
Pathology, General and Miscellaneous - Therapy \*12512  
Metabolism - General Metabolism; Metabolic Pathways \*13002  
Pathology, General and Miscellaneous - General \*12502  
Biochemical Studies - General \*10060  
General Biology - Symposia, Transactions and Proceedings of Conferences,  
Congresses, Review Annuals \*00520  
IT Major Concepts  
    Pharmacology  
IT Chemicals & Biochemicals  
    **AMPA receptors [alpha-amino-3-hydroxy-5-methyl-isoxazole propionate receptors]; noncompetitive quinazolinone AMPA receptor antagonists: molecular properties, pharmaceuticals, pharmacodynamics, pharmacological properties, synthesis**  
IT Miscellaneous Descriptors  
    drug discovery; structure-activity relationships; Meeting Abstract

=> d py all hitstr

L9 ANSWER 1 OF 4 CAPLUS COPYRIGHT 1999 ACS  
PY 1999  
1999  
1999  
1999  
AN 1999:175749 CAPLUS  
DN 130:218317  
TI AMPA antagonists for the treatment of dyskinesias associated with dopamine agonist therapy  
IN Chenard, Bertrand Leo; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.  
PA Pfizer Products Inc., USA  
SO Eur. Pat. Appl., 22 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
IC ICM A61K031-505  
ICI A61K031-505, A61K031-195, A61K031-15  
CC 1-11 (Pharmacology)  
Section cross-reference(s): 63  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900568	A2	19990310	EP 1998-307181	19980904
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 11158072	A2	19990615	JP 1998-245269	19980831
	AU 9883120	A1	19990318	AU 1998-83120	19980904
	CA 2246839	AA	19990305	CA 1998-2246839	19980908

PRAI US 1997-58098 19970905  
OS MARPAT 130:218317  
AB The invention relates to a method of treating dyskinesias assocd. with dopamine agonist therapy in a mammal which comprises administering to said mammal a compd., as defined herein, which is an antagonist of the AMPA receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease. One example compd. of the 212 claimed was (S)-3-(2-chlorophenyl)-2-[2-(5-diethylaminomethyl-2-fluorophenyl)vinyl]-6-fluoro-3H-quinazolin-4-one.  
ST AMPA antagonist dyskinesia dopamine agonist  
IT Drug delivery systems  
Parkinson's disease  
(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)  
IT AMPA receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)  
IT Dyskinesia (nervous system)  
(Parkinson's-assocd.; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)  
IT 51-61-6, Dopamine, biological studies 59-92-7, biological studies  
322-35-0, Benserazide 3257-47-4 28860-95-9, Carbidopa 199655-53-3  
199655-54-4 199655-56-6 199655-57-7 199655-58-8 199655-59-9  
199655-61-3 199655-62-4 199655-63-5 199655-64-6 199655-65-7  
199655-66-8 199655-67-9 199655-68-0 199655-69-1 199655-70-4  
199655-71-5 199655-72-6 199655-75-9 199655-76-0 199655-77-1  
199655-78-2 199655-80-6 199655-81-7 199655-82-8

199655-84-0	199655-86-2	199655-87-3	199655-88-4	199655-89-5
199655-90-8	199655-91-9	199656-00-3	199656-44-5	212710-60-6
212710-61-7	212710-62-8	212710-64-0	212710-65-1	212710-66-2
212710-70-8	212765-03-2	212850-63-0	212850-64-1	212850-72-1
212850-74-3	212850-78-7	212850-79-8	212850-80-1	212850-81-2
212850-82-3	212916-59-1	212916-65-9	217821-32-4	217821-33-5
217821-34-6	217821-35-7	217821-36-8	217821-37-9	217821-38-0
217821-39-1	217821-41-5	217821-42-6	217942-51-3	217942-54-6
217942-55-7	217942-57-9	217942-58-0	217942-60-4	217942-62-6
217942-63-7	217942-64-8	217942-66-0	217942-68-2	217942-69-3
217942-71-7	217942-72-8	217942-74-0	217942-76-2	217942-78-4
217942-86-4	217942-87-5	221151-74-2	221151-75-3	221151-81-1
221151-83-3	221151-84-4	221151-88-8	221151-95-7	221152-14-3
221152-18-7	221152-21-2	221152-23-4	221152-26-7	221152-29-0
221152-30-3	221152-31-4	221152-32-5	221152-34-7	221152-35-8
221152-36-9	221152-37-0	221152-38-1	221152-39-2	221152-40-5
221152-41-6	221152-42-7	221152-43-8	221152-44-9	221152-45-0
221152-46-1	221152-47-2	221152-48-3	221152-49-4	221152-50-7
221152-51-8	221152-52-9	221152-53-0	221152-54-1	221152-55-2
221152-56-3	221152-57-4	221152-58-5	221152-59-6	221152-60-9
221152-61-0	221152-62-1	221152-63-2	221167-22-2	221167-24-4
221167-27-7	221167-29-9	221167-33-5	221167-37-9	221167-44-8
221167-46-0	221167-49-3	221167-52-8	221167-54-0	221167-56-2
221167-59-5	221167-62-0	221167-63-1	221167-65-3	221167-66-4
221167-68-6	221167-70-0	221167-72-2	221167-73-3	221167-74-4
221167-75-5	221167-78-8	221167-79-9	221167-80-2	221167-81-3
221167-82-4	221167-83-5	221167-84-6	221167-85-7	221167-92-6
221167-95-9	221167-96-0	221167-97-1	221167-99-3	221168-01-0
221168-06-5	221168-10-1	221168-22-5	221168-25-8	221168-27-0
221168-39-4	221168-41-8	221168-42-9	221168-44-1	221168-46-3
221168-49-6	221168-52-1	221168-53-2	221168-58-7	221168-61-2
221168-64-5	221168-67-8	221168-70-3	221168-72-5	221168-74-7
221168-77-0	221168-78-1	221168-80-5	221168-82-7	221168-84-9
221168-86-1	221168-88-3	221177-80-6	221177-81-7	221177-82-8
221177-83-9	221177-84-0	221177-85-1	221177-86-2	221177-87-3
221177-88-4	221177-89-5	221177-90-8	221177-91-9	

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (AMPA antagonists for treatment of dyskinesias assocd. with dopamine  
 agonist therapy)

IT 77521-29-0, Ampa

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antagonists; AMPA antagonists for treatment of dyskinesias assocd.  
 with dopamine agonist therapy)

IT 9042-64-2, Dopa decarboxylase

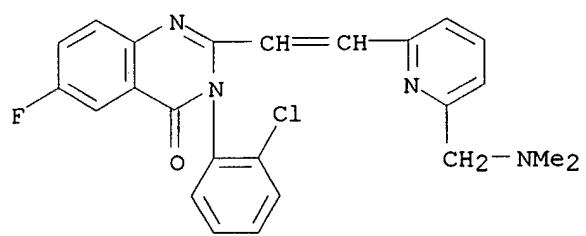
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; AMPA antagonists for treatment of dyskinesias assocd. with  
 dopamine agonist therapy)

IT 199655-81-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (AMPA antagonists for treatment of dyskinesias assocd. with dopamine  
 agonist therapy)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> d py all hitstr 2

L9 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS  
PY 1999  
1999  
1999  
1999  
AN 1999:175748 CAPLUS  
DN 130:209717  
TI Preparation of 3-(2-chlorophenyl)-2-[2-(6-diethylaminomethylpyridin-2-yl)vinyl]-6-fluoro-3H-quinazolin-4-one as an AMPA antagonist for the treatment of dyskinésias associated with dopamine agonist therapy.  
IN Chenard, Bertrand Leo; Greenamyre, John Timothy; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.  
PA Pfizer Products Inc., USA  
SO Eur. Pat. Appl., 6 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
IC ICM A61K031-505  
ICI A61K031-505, A61K031-195, A61K031-15  
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900567	A2	19990310	EP 1998-306661	19980820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2246560	AA	19990305	CA 1998-2246560	19980903
	JP 11139991	A2	19990525	JP 1998-249644	19980903
	AU 9883193	A1	19990318	AU 1998-83193	19980907
PRAI	US 1997-57965		19970905		
AB	A method for the treatment of dyskinésias assocd. with dopamine agonist therapy comprising administration of an AMPA antagonist is claimed (no data). Thus, 3-(2-chlorophenyl)-6-fluoro-2-methyl-4-(3H)-quinazolinone (prepn. given) was refluxed with 2,6-pyridinedicarboxaldehyde, ZnCl <sub>2</sub> , and Ac <sub>2</sub> O in dioxane to give 33% 6-[2-[3-(2-chlorophenyl)-6-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl]vinyl]pyridine-2-carboxaldehyde. This was stirred with Et <sub>2</sub> NH and NaBH(AcO) <sub>3</sub> in CH <sub>2</sub> Cl <sub>2</sub> to give 24% title compd. as the monomaleate salt.				
ST	chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolinone prepn AMPA antagonist; quinazolinone chlorophenyl-diethylaminomethylpyridinylvinyl prepn AMPA antagonist; dyskinésia treatment AMPA antagonist chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolinone				
IT	AMPA receptors RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study) (antagonists; prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolin-one as an AMPA antagonist for the treatment of dyskinésias assocd. with dopamine agonist therapy)				
IT	Dyskinésia (nervous system) (treatment; prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolin-one as an AMPA antagonist for the treatment of dyskinésias assocd. with dopamine agonist therapy)				
IT	<b>220931-86-2P</b> RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolin-				

one as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 199655-81-7

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolin-  
one as an AMPA antagonist for the treatment of dyskinesias assocd. with  
dopamine agonist therapy)

IT 59-92-7, L-Dopa, miscellaneous 322-35-0, Benserazide 28860-95-9,  
Carbidopa

RL: MSC (Miscellaneous)

(prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolin-  
one as an AMPA antagonist for the treatment of dyskinesias assocd. with  
dopamine agonist therapy)

IT 95-51-2, 2-Chloroaniline 109-89-7, reactions 320-98-9 5431-44-7,  
2,6-Pyridinedicarboxaldehyde

RL: RCT (Reactant)

(prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolin-  
one as an AMPA antagonist for the treatment of dyskinesias assocd. with  
dopamine agonist therapy)

IT 38520-78-4P 49579-12-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolin-  
one as an AMPA antagonist for the treatment of dyskinesias assocd. with  
dopamine agonist therapy)

IT 220931-86-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)

(prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolin-  
one as an AMPA antagonist for the treatment of dyskinesias assocd. with  
dopamine agonist therapy)

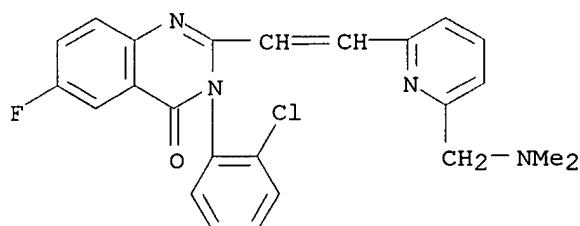
RN 220931-86-2 CAPIUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-  
pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX  
NAME)

CM 1

CRN 199655-81-7

CMF C24 H20 Cl F N4 O



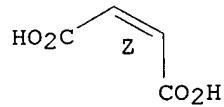
CM 2

CRN 110-16-7

CMF C4 H4 O4

CDES 2:Z

Double bond geometry as shown.

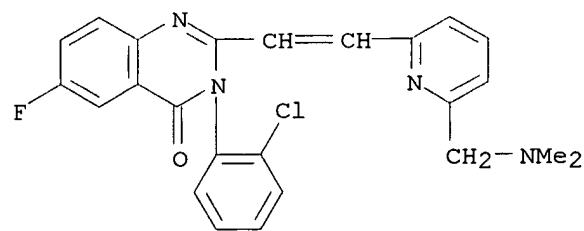


IT 199655-81-7

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(prepn. of chlorophenyl-diethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assoc'd. with dopamine agonist therapy)

RN 199655-81-7 CAPLUS

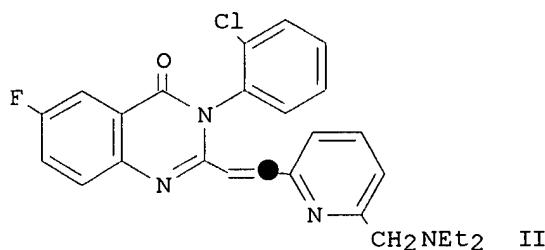
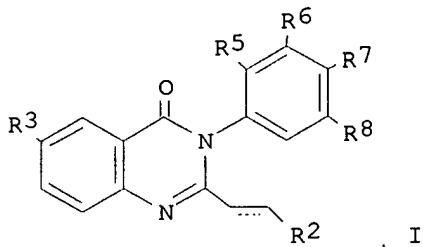
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> d py all hitstr 3

L9 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1999 ACS  
PY 1998  
1998  
AN 1998:608605 CAPLUS  
DN 129:230733  
TI Preparation of atropisomers of 3-aryl-4(3H)-quinazolinones and their use  
as AMPA-receptor antagonists  
IN Welch, Willard McKowan, Jr.; Devries, Keith M.  
PA Pfizer Products Inc., USA  
SO PCT Int. Appl., 81 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM C07D239-91  
ICS C07D401-06; C07D417-06; C07D401-14; C07D405-06; C07D413-06;  
A61K031-505; C07M007-00  
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 63  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9838173	A1	19980903	WO 1998-IB150	19980206
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9856768	A1	19980918	AU 1998-56768	19980206
PRAI	US 1997-38905		19970228		
	WO 1998-IB150		19980206		
OS	MARPAT	129:230733			
GI					



AB Title atropisomers [I; wherein R2 is an optionally substituted aryl or heteroaryl, R5 is alkyl, halo, CF<sub>3</sub>, alkoxy or alkylthio, R6, R7 and R8 are hydrogen or halo, and R3 is hydrogen, halo, CN, NO<sub>2</sub>, CF<sub>3</sub>, alkyl or alkoxy] are prep'd. and are useful as AMPA receptor antagonists, particularly in the treatment of neurodegenerative and CNS-trauma related conditions (no data). The title (S)-atropisomer II was prep'd. from 2-chloroaniline, 6-fluoro-2-methylquinoxalin-4-one which was prep'd. from hydrogenation, acetylation, and cyclization of 2-nitro-5-fluorobenzoic acid, followed by reaction with 2,6-pyridinedicarboxaldehyde, and diethylamine, and was column sepd.

ST quinazolinone prep'n; atropisomer quinazolinone sepn HPLC receptor antagonist

IT Separation

(HPLC column; prep'n. and sepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT AMPA receptors

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(antagonists; prep'n. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT 212850-63-0P 212850-64-1P 212850-65-2P 212850-66-3P 212850-68-5P  
 212850-70-9P 212850-72-1P 212850-73-2P 212850-74-3P 212850-75-4P  
 212850-76-5P 212850-77-6P 212850-78-7P 212850-79-8P 212850-80-1P  
 212850-81-2P 212850-82-3P 212916-59-1P 212916-60-4P 212916-61-5P  
 212916-62-6P 212916-63-7P 212916-64-8P 212916-65-9P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(antagonists; prep'n. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT 212850-63-0P 212850-64-1P 212850-65-2P 212850-66-3P 212850-68-5P  
 212850-70-9P 212850-72-1P 212850-73-2P 212850-74-3P 212850-75-4P  
 212850-76-5P 212850-77-6P 212850-78-7P 212850-79-8P 212850-80-1P  
 212850-81-2P 212850-82-3P 212916-59-1P 212916-60-4P 212916-61-5P  
 212916-62-6P 212916-63-7P 212916-64-8P 212916-65-9P

(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT	10200-43-8P	49579-12-6P	68683-04-5P	78441-69-7P	82586-66-1P
	113732-84-6P	141567-53-5P	174608-36-7P	194473-04-6P	199599-68-3P
	199655-35-1P	199655-36-2P	199655-54-4P	199655-55-5P	199655-57-7P
	199655-61-3P	199655-62-4P	199655-63-5P	199655-65-7P	199655-66-8P
	199655-67-9P	199655-68-0P	199655-69-1P	199655-70-4P	199655-71-5P
	199655-72-6P	199655-73-7P	199655-74-8P	199655-75-9P	199655-76-0P
	199655-77-1P	199655-78-2P	199655-79-3P	199655-80-6P	
	<b>199655-81-7P</b>	199655-82-8P	199655-83-9P	199655-84-0P	
	199655-86-2P	199655-87-3P	199655-88-4P	199655-89-5P	199655-90-8P
	199655-91-9P	199655-92-0P	199655-93-1P	199655-96-4P	199655-97-5P
	199655-98-6P	199655-99-7P	199656-02-5P	199656-03-6P	199656-04-7P
	199656-05-8P	199656-06-9P	199656-28-5P	199656-29-6P	199656-30-9P
	199656-31-0P	199656-32-1P	199656-33-2P	199656-34-3P	199656-35-4P
	199656-40-1P	212764-92-6P	212764-93-7P	212764-94-8P	212764-95-9P
	212764-96-0P	212764-97-1P	212764-99-3P	212765-00-9P	212765-01-0P
	212765-02-1P	212765-03-2P	212765-05-4P	212765-06-5P	212765-07-6P
	212765-08-7P	212765-09-8P	212765-10-1P	212765-11-2P	212765-12-3P
	212765-13-4P	212765-15-6P	212765-16-7P	212765-19-0P	212765-20-3P
	212765-21-4P	212765-22-5P	212765-23-6P	212765-24-7P	212765-25-8P
	212765-26-9P	212765-27-0P	212765-28-1P	212772-14-0P	

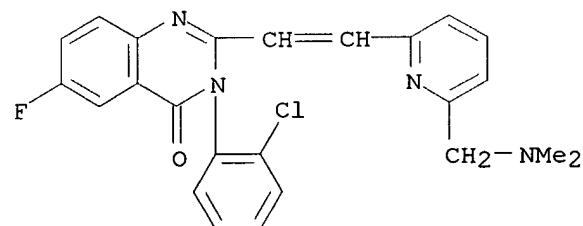
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT **199655-81-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)

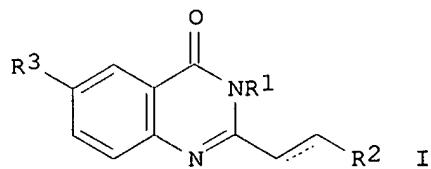


=> d py all hitstr 4

L9 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS  
PY 1997  
1997  
1997  
1999  
1999  
1999  
1999  
AN 1997:752948 CAPLUS  
DN 128:34774  
TI Preparation of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists.  
IN Elliott, Mark Leonard; Welch, Willard Mckowan Jr  
PA Pfizer Inc., USA; Elliott, Mark Leonard; Welch, Willard Mckowan Jr.  
SO PCT Int. Appl., 77 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM C07D401-06  
ICS C07D401-04; C07D401-14; C07D405-06; C07D403-06; C07D239-91;  
C07D417-14; C07D417-06; A61K031-505  
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743276	A1	19971120	WO 1997-IB134	19970217
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2252907	AA	19971120	CA 1997-2252907	19970217
	AU 9715549	A1	19971205	AU 1997-15549	19970217
	EP 901487	A1	19990317	EP 1997-901749	19970217
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	CN 1218464	A	19990602	CN 1997-194654	19970217
	NO 9805293	A	19990113	NO 1998-5293	19981113
PRAI	US 1996-17738		19960515		
	WO 1997-IB134		19970217		
OS	MARPAT	128:34774			
GI					



AB Title compds. [I; R1 = (substituted) Ph, pyridyl; R2 = (substituted) Ph, 5-6 membered heterocyclyl; R3 = H, halo, cyano, NO<sub>2</sub>, CF<sub>3</sub>, alkyl, alkoxy], were prepd. Thus, 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylvinyl)-3H-quinazolin-4-one was hydrogenated in EtOAc over Pd/C to give 100% 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylethyl)-3H-quinazolin-4-one. Tested I inhibited AMPA receptor activation-induced 45Ca<sup>2+</sup> uptake with IC<sub>50</sub> <5 .mu.M.

ST quinazolinone prepn AMPA receptor antagonist; nervous system agents quinazolinone

IT Nervous system agents

Neurotransmitter antagonists

(prep. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT 3257-47-4P 199655-35-1P 199655-36-2P 199655-37-3P 199655-38-4P  
 199655-39-5P 199655-40-8P 199655-41-9P 199655-42-0P 199655-43-1P  
 199655-44-2P 199655-45-3P 199655-46-4P 199655-47-5P 199655-48-6P  
 199655-49-7P 199655-50-0P 199655-51-1P 199655-52-2P 199655-53-3P  
 199655-54-4P 199655-55-5P 199655-56-6P 199655-57-7P 199655-58-8P  
 199655-59-9P 199655-60-2P 199655-61-3P 199655-62-4P 199655-63-5P  
 199655-64-6P 199655-65-7P 199655-66-8P 199655-67-9P 199655-68-0P  
 199655-69-1P 199655-70-4P 199655-71-5P 199655-72-6P 199655-73-7P  
 199655-74-8P 199655-75-9P 199655-76-0P 199655-77-1P 199655-78-2P  
 199655-79-3P 199655-80-6P **199655-81-7P** 199655-82-8P  
 199655-83-9P 199655-84-0P 199655-85-1P 199655-86-2P 199655-87-3P  
 199655-88-4P 199655-89-5P 199655-90-8P 199655-91-9P 199655-92-0P  
 199655-93-1P 199655-94-2P 199655-95-3P 199655-96-4P 199655-97-5P  
 199655-98-6P 199655-99-7P 199656-00-3P 199656-01-4P 199656-02-5P  
 199656-03-6P 199656-04-7P 199656-05-8P 199656-06-9P 199656-07-0P  
 199656-08-1P 199656-09-2P 199656-10-5P 199656-11-6P 199656-12-7P  
 199656-13-8P 199656-14-9P 199656-15-0P 199656-16-1P 199656-17-2P  
 199656-18-3P 199656-19-4P 199656-20-7P 199656-21-8P 199656-22-9P  
 199656-23-0P 199656-24-1P 199656-25-2P 199656-26-3P 199656-27-4P  
 199656-28-5P 199656-29-6P 199656-30-9P 199656-31-0P 199656-32-1P  
 199656-33-2P 199656-34-3P 199656-35-4P 199656-36-5P 199656-37-6P  
 199656-38-7P 199656-39-8P 199656-40-1P 199656-41-2P 199656-44-5P  
 199656-45-6P 199656-46-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prep. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT 95-51-2, 2-Chloroaniline 320-98-9 340-57-8 5431-44-7,  
 2,6-Pyridinedicarboxaldehyde 20949-84-2, 2-Methylthiazole-4-carboxaldehyde 49579-01-3 49579-08-0 199599-68-3 199656-42-3  
 199656-43-4

RL: RCT (Reactant)

(prep. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT 38520-78-4P 49579-12-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prep. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

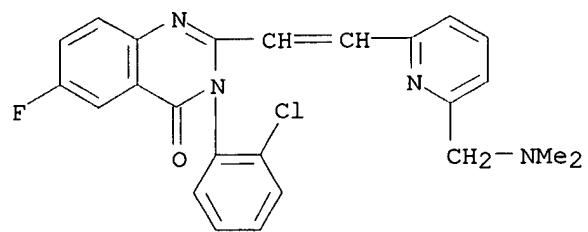
IT **199655-81-7P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prep. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> d std bib ab clm

L14 ANSWER 1 OF 1 USPATFULL  
AN 97:86624 USPATFULL  
TI Excitatory amino acid receptor antagonists  
IN Arnold, M. Brian, Franklin, IN, United States  
Augenstein, Nancy K., Indianapolis, IN, United States  
Lunn, William H. W., Indianapolis, IN, United States  
Ornstein, Paul L., Indianapolis, IN, United States  
Schoepp, Darryle D., Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.  
corporation)  
PI US 5670516 19970923  
AI US 1995-456439 19950601 (8)  
RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994, now abandoned  
which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993,  
now patented, Pat. No. US 5399696 which is a division of Ser. No. US  
1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957  
DT Utility  
LN.CNT 3909  
INCL INCLM: 514/307.000  
INCLS: 546/147.000  
NCL NCLM: 514/307.000  
NCLS: 546/147.000  
IC [6]  
ICM: C07D215-14  
ICS: A61K031-47  
EXF 546/23; 546/146; 546/147; 546/148; 546/150; 514/307  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AN 97:86624 USPATFULL  
TI Excitatory amino acid receptor antagonists  
IN Arnold, M. Brian, Franklin, IN, United States  
Augenstein, Nancy K., Indianapolis, IN, United States  
Lunn, William H. W., Indianapolis, IN, United States  
Ornstein, Paul L., Indianapolis, IN, United States  
Schoepp, Darryle D., Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.  
corporation)  
PI US 5670516 19970923  
AI US 1995-456439 19950601 (8)  
RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994, now abandoned  
which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993,  
now patented, Pat. No. US 5399696 which is a division of Ser. No. US  
1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957  
DT Utility  
EXNAM Primary Examiner: Davis, Zinna Northington  
LREP Hay, Martin A.; Leeds, James P.  
CLMN Number of Claims: 42  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 3909  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB This invention provides novel decahydroisoquinoline compounds which are  
useful as excitatory amino acid receptor antagonists and in the  
treatment of neurological disorders. This invention also provides  
synthetic methods for preparing decahydroisoquinolines, as well as,  
novel intermediates in the synthesis thereof.  
CLM What is claimed is:  
1. A compound of the formula ##STR87## wherein: R.sup.1 is hydrogen,

C.<sub>sub.1</sub> -C.<sub>sub.10</sub> alkyl, arylalkyl, alkoxycarbonyl or acyl; R.<sub>sup.2</sub> is hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.6</sub> alkyl, substituted alkyl, cycloalkyl, or arylalkyl; R.<sub>sup.3</sub> is CO.<sub>sub.2</sub> H, SO.<sub>sub.3</sub> H, CONHSO.<sub>sub.2</sub> R.<sub>sup.8</sub>, or a group of formula ##STR88## W is (CH.<sub>sub.2</sub>).<sub>sub.n</sub>, S, SO, SO.<sub>sub.2</sub>; Y is CHR.<sub>sup.7</sub>, NR.<sub>sup.4</sub>, O, S, SO, or SO.<sub>sub.2</sub>; Z is NR.<sub>sup.6</sub>, CHR.<sub>sup.7</sub>, or CH; or W and Y together are HC.dbd.CH or C.tbd.C, or Y and Z together are HC.dbd.CH or C.tbd.C; R.<sub>sup.4</sub> is hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl, phenyl, or acyl; R.<sub>sup.5</sub> is hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl, CF.<sub>sub.3</sub>, phenyl, hydroxy, amino, bromo, iodo, or chloro; R.<sub>sup.6</sub> is acyl; R.<sub>sup.7</sub> is independently hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl, phenyl, or substituted phenyl; R.<sub>sup.8</sub> is C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl or tetrazole-5-yl; and n is 0, 1, or 2; provided that when Y is NR.<sub>sup.4</sub>, O, S, SO, or SO.<sub>sub.2</sub>, W is (CH.<sub>sub.2</sub>).<sub>sub.n</sub> and Z is CHR.<sub>sup.7</sub> or CH; further provided that when W is S, SO, or SO.<sub>sub.2</sub>, Y is CHR.<sub>sup.7</sub>, Z is CHR.<sub>sup.7</sub> or CH, or Y and Z together are HC.dbd.CH or C.tbd.C; further provided that when W and Z are CH.<sub>sub.2</sub>, Y is not S; further provided that when W and Y together are HC.dbd.CH or C.tbd.C, Z is CHR.<sub>sub.7</sub>; or a pharmaceutically acceptable salt thereof.

2. A compound of claim 1 wherein: R.<sub>sup.1</sub> is hydrogen or alkoxycarbonyl; R.<sub>sup.2</sub> is hydrogen or C.<sub>sub.1</sub> -C.<sub>sub.6</sub> alkyl; R.<sub>sup.3</sub> is a group selected from the group consisting of CO.<sub>sub.2</sub> H, SO.<sub>sub.3</sub> H, CONHSO.<sub>sub.2</sub> R.<sub>sup.8</sub>, and ##STR89## W is S or (CH.<sub>sub.2</sub>).<sub>sub.n</sub>; n is 0, 1, or 2; Y is CHR.<sub>sup.7</sub>, S, SO.<sub>sub.2</sub> or O; Z is CHR.<sub>sup.7</sub> or NR.<sub>sup.6</sub>; or Y and Z together are HC.dbd.CH; R.<sub>sup.6</sub> is formyl; R.<sub>sup.7</sub> is independently hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl, or phenyl; R.<sub>sup.8</sub> is C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl or tetrazole-5-yl; or a pharmaceutically acceptable salt thereof.

3. A compound of claim 2 wherein R.<sub>sup.1</sub> and R.<sub>sup.2</sub> are hydrogen, or a pharmaceutically acceptable salt thereof.

4. A compound of claim 2 wherein: R.<sub>sup.1</sub> is hydrogen or alkoxycarbonyl; R.<sub>sup.2</sub> is hydrogen or C.<sub>sub.1</sub> -C.<sub>sub.6</sub> alkyl; R.<sub>sup.3</sub> is a group selected from the group consisting of SO.<sub>sub.3</sub> H and a group of the formula ##STR90## W is S, SO.<sub>sub.2</sub> or (CH.<sub>sub.2</sub>).<sub>sub.n</sub>; n is 0, 1, or 2; Y is CHR.<sub>sup.7</sub>, S, or SO.<sub>sub.2</sub>; Z is CHR.<sub>sup.7</sub>; R.<sub>sup.5</sub> is hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl, or CF.<sub>sub.3</sub>; and R.<sub>sup.7</sub> is hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl, or phenyl; or a pharmaceutically acceptable salt thereof.

5. A compound of claim 4 wherein: R.<sub>sup.1</sub> and R.<sub>sup.2</sub> are hydrogen, or a pharmaceutically acceptable salt thereof.

6. A compound of claim 4 wherein: R.<sub>sup.1</sub> and R.<sub>sup.2</sub> are hydrogen; R.<sub>sup.3</sub> is a group selected from the group of the formula ##STR91## W is (CH.<sub>sub.2</sub>).<sub>sub.n</sub>; n is 0; Y is CHR.<sub>sup.7</sub>, S, or SO.<sub>sub.2</sub>; Z is CHR.<sub>sup.7</sub>; R.<sub>sup.5</sub> is hydrogen or C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl; and R.<sub>sup.7</sub> is hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.4</sub> alkyl, or phenyl; or a pharmaceutically acceptable salt thereof.

7. A compound of claim 6 wherein R.<sub>sup.3</sub> is a group of the formula ##STR92## or a pharmaceutically acceptable salt thereof.

8. A compound of claim 6 wherein R.<sub>sup.3</sub> is a group of the formula ##STR93## or a pharmaceutically acceptable salt thereof.

9. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

10. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

11. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

12. The compound of claim 6 which is (3S,4aR,6S,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

13. The compound of claim 6 which is 6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

14. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

15. The compound of claim 6 which is 6-[(1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

16. The compound of claim 6 which is (3S,4aR,6S,8aR)-6-[(1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

17. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

18. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

19. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

20. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

21. A method of blocking the **AMPA** excitatory amino acid receptor in mammals which comprises administering to a mammal requiring decreased excitatory amino acid neurotransmission a pharmaceutically-effective amount of a compound of claim 1.

22. A method of blocking the **AMPA** excitatory amino acid receptor in mammals which comprises administering to a mammal requiring decreased excitatory amino acid neurotransmission a pharmaceutically-effective amount of a compound of claim 6.

23. A method of treating a neurological disorder in a patient, which comprises administering to a patient in need thereof, an effective amount of a compound of claim 1.

24. The method of claim 23 wherein said neurological disorder is

cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive dyskinesia.

25. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, cardiac arrest, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, chronic pain, psychosis, emesis, muscular spasms, amyotrophic lateral sclerosis, or ocular damage and retinopathy.

26. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, ocular damage and retinopathy, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, or chronic pain.

27. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, or ocular damage and retinopathy.

28. A method of treating a neurological disorder in a patient, which comprises administering to a patient in need thereof, an effective amount of a compound of claim 6.

29. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive dyskinesia.

30. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, cardiac arrest, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, chronic pain, psychosis, emesis, muscular spasms, amyotrophic lateral sclerosis, or ocular damage and retinopathy.

31. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, ocular damage and retinopathy, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, or chronic pain.

32. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, or ocular damage and retinopathy.

33. A method of producing analgesia in mammals which comprises administering to a mammal an effective amount of a compound of claim 1.

34. A method of producing analgesia in mammals which comprises administering to a mammal an effective amount of a compound of claim 6.

35. A pharmaceutical formulation comprising a compound of claim 1 and a pharmaceutically-acceptable carrier, diluent, or excipient.

36. A pharmaceutical formulation comprising a compound of claim 6 and a pharmaceutically-acceptable carrier, diluent, or excipient.

37. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

38. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]-decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt.

39. A formulation according to claim 36 wherein the compound is 6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

40. A formulation according to claim 35 wherein the compound is 6-[ (1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]-decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

41. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

42. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

=> d 134 std bib ab hit

L34 ANSWER 1 OF 5 USPATFULL  
AN 97:16213 USPATFULL  
TI Isoquinolinyl-carboxylic acid receptor antagonists compounds  
IN Huff, Bret, Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.  
corporation)  
PI US 5606062 19970225 ---  
AI US 1995-457556 19950601 (8)  
RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994 which is a  
division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented,  
Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780,  
filed on 3 Sep 1992, now patented, Pat. No. US 5284957  
DT Utility  
LN.CNT 3730  
INCL INCLM: 546/147.000  
NCL NCLM: 546/147.000  
IC [6]  
ICM: C07D217-16  
EXF 546/146; 546/147  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AN 97:16213 USPATFULL  
TI Isoquinolinyl-carboxylic acid receptor antagonists compounds  
IN Huff, Bret, Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.  
corporation)  
PI US 5606062 19970225 ---  
AI US 1995-457556 19950601 (8)  
RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994 which is a  
division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented,  
Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780,  
filed on 3 Sep 1992, now patented, Pat. No. US 5284957  
DT Utility  
EXNAM Primary Examiner: Davis, Zinna Northington  
LREP Hay, Martin A.; Leeds, James P.  
CLMN Number of Claims: 6  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 3730  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB This invention provides novel decahydroisoquinoline compounds which are  
useful as excitatory amino acid receptor antagonists and in the  
treatment of neurological disorders. This invention also provides  
synthetic methods for preparing decahydroisoquinolines, as well as,  
novel intermediates in the synthesis thereof.  
PI US 5606062 19970225 ---  
SUMM Excitatory amino acid excitotoxicity has been implicated in the  
pathophysiology of a number of neurological disorders. This  
excitotoxicity has been implicated in the pathophysiology of acute and  
chronic neurodegenerative conditions including cerebral deficits  
subsequent to cardiac bypass surgery and grafting, stroke, cerebral  
ischemia, spinal cord trauma, head trauma, Alzheimer's Disease,  
Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced  
dementia, perinatal hypoxia, cardiac arrest, hypoglyemic neuronal  
damage, ocular damage and retinopathy, and idiopathic and drug-induced  
Parkinson's Disease. Other neurological conditions, that are caused by  
glutamate dysfunction, require neuromodulation. These other neurological  
conditions include muscular spasms, migraine headaches, urinary

incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive **dyskinesia**. The use of a neuroprotective agent, such as an AMPA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The EAA antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to the excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d 134 std bib ab hit 2

L34 ANSWER 2 OF 5 USPATFULL  
AN 96:53325 USPATFULL  
TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists  
IN Ornstein, Paul L., Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)  
PI US 5527810 19960618 <--  
AI US 1994-255590 19940608 (8)  
RLI Division of Ser. No. US 1992-972679, filed on 6 Nov 1992, now patented, Pat. No. US 5356902  
DT Utility  
LN.CNT 1477  
INCL INCLM: 514/307.000  
INCLS: 546/144.000; 546/147.000  
NCL NCLM: 514/307.000  
NCLS: 546/144.000; 546/147.000  
IC [6]  
ICM: A01N043-42  
ICS: C07D217-00  
EXF 546/144; 546/147; 514/307  
AN 96:53325 USPATFULL  
TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists  
IN Ornstein, Paul L., Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)  
PI US 5527810 19960618 <--  
AI US 1994-255590 19940608 (8)  
RLI Division of Ser. No. US 1992-972679, filed on 6 Nov 1992, now patented, Pat. No. US 5356902  
DT Utility  
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Covington, Raymond  
LREP Hay, Martin A.; Leeds, James P.  
CLMN Number of Claims: 12  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1477  
AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders. This invention also provides synthetic methods for preparing decahydroisoquinolines.  
PI US 5527810 19960618 <--  
SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of acute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive

**dyskinesia**. The use of a neuroprotective agent, such as an AMPA or NMDA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The excitatory amino acid antagonists are also useful as analgesic agents.

- SUMM Further embodiments of the invention include a method of blocking the AMPA or the NMDA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to these excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.
- SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.
- CLM What is claimed is:
2. The method of claim 1 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**.
7. The method of claim 6 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**.

=> d 134 std bib ab hit 3

L34 ANSWER 3 OF 5 USPATFULL  
AN 95:78190 USPATFULL  
TI Aryl-spaced decahydroisoquinoline-3-carboxylic acids as excitatory amino acid receptor antagonists  
IN Ornstein, Paul L., Carmel, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)  
PI US 5446051 19950829 <--  
AI US 1994-251809 19940531 (8)  
DT Utility  
LN.CNT 1093  
INCL INCLM: 514/307.000  
INCLS: 546/022.000; 546/147.000  
NCL NCLM: 514/307.000  
NCLS: 546/022.000; 546/147.000  
IC [6]  
ICM: C07D217-06  
ICS: A61K031-47  
EXF 546/22; 546/146; 546/147; 514/307  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AN 95:78190 USPATFULL  
TI Aryl-spaced decahydroisoquinoline-3-carboxylic acids as excitatory amino acid receptor antagonists  
IN Ornstein, Paul L., Carmel, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)  
PI US 5446051 19950829 <--  
AI US 1994-251809 19940531 (8)  
DT Utility  
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Davis, Zinna N.  
LREP Hay, Martin A.; Dodd, Thomas J.; Boone, David E.  
CLMN Number of Claims: 40  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1093  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention provides novel decahydroisoquinoline derivatives which are useful as excitatory amino acid antagonists. The invention also provides for methods of using these derivatives to treat various neurological disorders.  
PI US 5446051 19950829 <--  
SUMM Use of Formula (I) compounds as AMPA selective antagonists is seen as potentially beneficial in treating a number of neurodegenerative conditions including, but not limited to Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, cognitive disorders, Parkinson's Disease, anxiety, emesis, brain edema, chronic pain and tardive **dyskinesia**, among others. Formula (I) compounds are also contemplated for use to abate cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, and spinal cord and brain trauma injuries. Further, Formula (I) compounds are contemplated for use as analgesic agents.  
SUMM The formula I compounds of the present invention are also believed to

have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d 134 std bib ab hit 4

L34 ANSWER 4 OF 5 USPATFULL  
AN 95:25041 USPATFULL  
TI Isoquinolinyl compounds which are intermediates  
IN Arnold, M. Brian, Franklin, IN, United States  
Augenstein, Nancy K., Indianapolis, IN, United States  
Lunn, William H. W., Indianapolis, IN, United States  
Ornstein, Paul L., Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.  
corporation)  
PI US 5399696 19950321 <--  
AI US 1993-111747 19930825 (8)  
RLI Division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented,  
Pat. No. US 5284957  
DT Utility  
LN.CNT 3727  
INCL INCLM: 546/147.000  
NCL NCLM: 546/147.000  
IC [6]  
ICM: C07D217-02  
EXF 546/147; 546/15  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AN 95:25041 USPATFULL  
TI Isoquinolinyl compounds which are intermediates  
IN Arnold, M. Brian, Franklin, IN, United States  
Augenstein, Nancy K., Indianapolis, IN, United States  
Lunn, William H. W., Indianapolis, IN, United States  
Ornstein, Paul L., Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.  
corporation)  
PI US 5399696 19950321 <--  
AI US 1993-111747 19930825 (8)  
RLI Division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented,  
Pat. No. US 5284957  
DT Utility  
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Davis, Zinna N.  
LREP Leeds, James P.  
CLMN Number of Claims: 4  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 3727  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB This invention provides novel decahydroisoquinoline compounds which are  
useful as excitatory amino acid receptor antagonists and in the  
treatment of neurological disorders. This invention also provides  
synthetic methods for preparing decahydroisoquinolines, as well as,  
novel intermediates in the synthesis thereof.  
PI US 5399696 19950321 <--  
SUMM Excitatory amino acid excitotoxicity has been implicated in the  
pathophysiology of a number of neurological disorders. This  
excitotoxicity has been implicated in the pathophysiology of acute and  
chronic neurodegenerative conditions including cerebral deficits  
subsequent to cardiac bypass surgery and grafting, stroke, cerebral  
ischemia, spinal cord trauma, head trauma, Alzheimer's Disease,  
Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced  
dementia, perinatal hypoxia, cardiac arrest, hypoglyemic neuronal  
damage, ocular damage and retinopathy, and idiopathic and drug-induced  
Parkinson's Disease. Other neurological conditions, that are caused by

glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive **dyskinesia**. The use of a neuroprotective agent, such as an AMPA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The EAA antagonists are also useful as analgesic agents.

- SUMM Further embodiments of the invention include a method of blocking the AMPA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to the excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.
- SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d 134 std bib ab hit 5

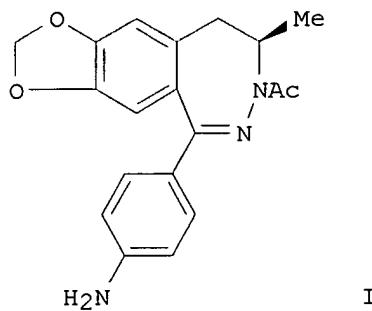
L34 ANSWER 5 OF 5 USPATFULL  
AN 94:91059 USPATFULL  
TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists  
IN Ornstein, Paul L., Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)  
PI US 5356902 19941018 <--  
AI US 1992-972679 19921106 (7)  
DT Utility  
LN.CNT 1383  
INCL INCLM: 514/307.000  
INCLS: 546/144.000; 546/147.000  
NCL NCLM: 514/307.000  
NCLS: 546/144.000; 546/147.000  
IC [5]  
ICM: A01N043-42  
ICS: C07D217-00  
EXF 546/147; 546/144; 514/307  
AN 94:91059 USPATFULL  
TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists  
IN Ornstein, Paul L., Indianapolis, IN, United States  
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)  
PI US 5356902 19941018 <--  
AI US 1992-972679 19921106 (7)  
DT Utility  
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Covington, Raymond  
LREP Leeds, James P.  
CLMN Number of Claims: 16  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 1383  
AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders.  
PI US 5356902 19941018 <--  
SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of a acute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive dyskinesia. The use of a neuroprotective agent, such as an AMPA or NMDA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The excitatory amino acid antagonists are also useful as analgesic agents.

- SUMM Further embodiments of the invention include a method of blocking the AMPA or the NMDA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to these excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.
- DETD The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d 4 py all

L11 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS  
PY 1996  
1996  
1996  
1996  
1996  
1998  
1996  
1996  
1996  
1996  
1996  
1996  
1998  
AN 1996:307308 CAPLUS  
DN 124:343338  
TI Physical form of dihydro-2,3-benzodiazepine derivative useful as an  
**AMPA antagonist**  
IN Anderson, Benjamin Alan; Hansen, Marvin Martin; Vicenzi, Jeffrey Thomas;  
Varie, David Lee; Zmijewski, Milton Joseph, Jr.; Harkness, Allen Robert  
PA Lilly, Eli, and Co., USA  
SO Eur. Pat. Appl., 19 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
IC ICM C07D491-056  
ICS A61K031-55  
ICI C07D491-056, C07D317-00, C07D243-00  
CC 28-21 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1, 16, 63  
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 699676	A1	19960306	EP 1995-306048	19950830
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, MC, NL, PT, SE				
	NO 9503395	A	19960301	NO 1995-3395	19950830
	CA 2157247	AA	19960301	CA 1995-2157247	19950830
	FI 9504065	A	19960301	FI 1995-4065	19950830
	AU 9530356	A1	19960314	AU 1995-30356	19950830
	AU 696243	B2	19980903		
	JP 08092255	A2	19960409	JP 1995-221572	19950830
	CN 1122338	A	19960515	CN 1995-109526	19950830
	HU 72673	A2	19960528	HU 1995-2547	19950830
	BR 9503844	A	19960910	BR 1995-3844	19950830
	IL 115101	A1	19981227	IL 1995-115101	19950830
PRAI	US 1994-298645	19940831			
	US 1995-413024	19950328			
	US 1994-289645	19940831			
OS	CASREACT	124:343338			
GI					



- AB A phys. form of (R)-7-acetyl-5-(4-aminophenyl)-8,9-dihydro-8-methyl-7H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (I) is disclosed, having an x-ray powder diffraction pattern with d spacings at 10.61, 8.83, 6.78, 5.83, 4.13 and 3.74 .ANG.. The compd. is an **AMPA antagonist** (no data), useful for treating a variety of CNS and other disorders. I is prepd. in approx. 7 steps with several variations. For example, reductive fermn. of (3,4-methylenedioxophenyl)acetone with *Zygosaccharomyces rouxii* ATCC 14462 gave (S)-.alpha.-methyl-1,3-benzodioxole-5-ethanol in 85-90% isolated yield and 100% ee. This underwent cyclization with p-nitrobenzaldehyde to a benzopyran deriv. (87-93%), atm. hydroxylation in DMSO-DMF to a cyclic hemiacetal, ring cleavage by AcHNH2 to an alc./hydrazone (91%), mesylation of the alc. (87%), cyclization of the mesylate/hydrazone (90%), and redn. of the nitro group with aq. K formate over Pd/C (93%), giving form IV of I. Two chem. variants of the 1st step, and preps. of forms I, II, and III of I using different redn. procedures in the last step, are also described.
- ST benzodiazepine prep **AMPA antagonist**;
- IT dioxolobenzodiazepine acetylaminophenylidihromethyl form IV prep
- IT Analgesics
- IT Anticonvulsants and Antiepileptics
- IT Antiemetics
- IT Anxiolytics
- IT Muscle relaxants
- IT Nervous system agents
- IT (prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Saccharomyces rouxii
- IT (reductive fermn. of (methylenedioxophenyl)acetone; prep. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Drug dependence
- IT Parkinsonism
- IT (treatment; prep. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Mental disorder
- IT (Alzheimer's disease, treatment; prep. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Tranquilizers and Neuroleptics
- IT (antipsychotics, prep. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Mental disorder
- IT (dementia, treatment; prep. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Nervous system
- IT (disease, Huntington's chorea, treatment; prep. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)

antagonist)

IT Nervous system  
(disease, amyotrophic lateral sclerosis, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Bladder  
(disease, incontinence, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Nervous system  
(disease, tardive **dyskinesia**, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Brain, disease  
(edema, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Neurotransmitter antagonists  
(glutamatergic, prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Receptors  
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)  
(glutamatergic, AMPA-binding, prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Eye, disease  
(injury, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Brain, disease  
(ischemia, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Headache  
(migraine, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Eye, disease  
(retinopathy, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT Brain, disease  
(stroke, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT 172542-26-6P, (S)-.alpha.-Methyl-1,3-benzodioxole-5-ethanol  
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(intermediate; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT 161832-64-0P 172542-27-7P 172542-28-8P 172542-29-9P 172542-30-2P  
172542-31-3P 172721-25-4P 172721-26-5P 172721-27-6P 176777-96-1P  
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(intermediate; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT 161832-65-1P  
RL: BAC (Biological activity or effector, except adverse); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor antagonist)

IT 124-63-0, Methanesulfonyl chloride 555-16-8, p-Nitrobenzaldehyde, reactions 1068-57-1, Acetic hydrazide 2635-13-4, 4-Bromo-1,2-methylenedioxybenzene 4676-39-5, (3,4-Methylenedioxyphenyl)acetone 16088-62-3, (S)-(-)-Propylene oxide, reactions

RL: RCT (Reactant)  
(starting material; prepn. of dihydro-2,3-benzodiazepine deriv. phys.  
form as **AMPA** receptor **antagonist**)